PUBLIC HEALTH REPORTS

In this issue

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frontispiece

Research achievements in arthritis and the metabolic diseases during the past decade are reviewed in the progress report of the National Institute of Arthritis and Metabolic Diseases appearing on pages 788–792. (Photograph by Jerry Hecht)

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SYNOPSES

POSKANZER, DAVID C. (Massachusetts General Hospital, Boston), and BEADENKOPF, WILLIAM G.: ***Waterborne infectious hepatitis epidemic from a chlorinated municipal supply. Public Health Reports, Vol. 76, September 1961, pp. 745–751.***

An epidemic of 83 cases of infectious hepatitis with jaundice occurred in two neighboring New York State communities between November 21, 1956, and February 1, 1957. Seventy cases occurred within the first 30 days of the epidemic. The two communities, although 2 miles apart, had a common water supply. As an emergency measure water was taken from a stream potentially subject to pollution. It was chlorinated but not otherwise treated.

Only 2 of the first 70 patients did not reside on the water supply. The distribution in time of the cases is consistent with a common-source epidemic. Milk, food, contact, insects, hepatotoxins, and parenteral inoculations appeared very unlikely as common sources of infection. It is concluded that the epidemic of infectious hepatitis was waterborne through the emergency water supply, despite the fact that the water was chlorinated.

MACDONALD, GEORGE: (Ross Institute of Tropical Hygiene, London), ***Epidemiologic models in studies of vector-borne diseases. Public Health Reports, Vol. 76, September 1961, pp. 753–764.***

The steps in the creation of an epidemiologic model are examined individually, from the quantitative statement of the factors involved to the development of an expression for equilibrium and of the sensitivity of this equilibrium to changes in its controlling factors, whether they occur naturally or are artificially produced as preventive measures. The use of a model to clarify the epidemiology of a disease, as a guide to research processes, and in considering the strategy of control, is discussed on the basis of malaria.

Extension of this process to other conditions is considered, showing that it could usefully be applied to filariasis and schistosomiasis, though the first result of examination of prototypes reveals significant gaps in quantitative knowledge which need remedy. It would be simple to extend this method to the arthropod-borne virus diseases, with considerable illumination of the present epidemiologic picture. The mathematical expressions for malaria, schistosomiasis, and for a hypothetical arthropod-borne virus infection are given.

FROTHINGHAM, THOMAS E. (Public Health Research Institute of the City of New York), and SANYAKORN, CHAIYAN K.: ***Parainfluenza viruses in southern Louisiana. Public Health Reports, Vol. 76, September 1961, pp. 765–770.***

Thirteen hemadsorbing agents were isolated from 343 infants and children hospitalized in New Orleans, La., between May 1959 and April 1960. Six of these isolates were typed as hemadsorption virus type 1 (parainfluenza type 3), three as influenza type A2, and four were unidentified.

Serums from 380 other residents of southern Louisiana were tested for neutralizing antibodies to four of the parainfluenza viruses. The percentages of these individuals showing antibodies to HA1, croup associated, HA2, and Sendai viruses were 75, 37, 19, and 9, respectively.

The findings of this study as well as those of similar studies reported in the literature indicate the presence in southern Louisiana of HA1, CA, and HA2 viruses but not of Sendai.

ANGELOTTI, ROBERT (Public Health Service), BAILEY, GEORGE C., FOTER, MILTON, J., and LEWIS, KEITH H.: ***Salmonella infantis isolated from ham in food poisoning incident. Public Health Reports, Vol. 76, September 1961, pp. 771–776.***

Investigation of an outbreak of gastroenteritis affecting eight members of a family revealed that the only food eaten in common was ham. Bacteriological examination of the ham disclosed that the organisms of significance present in large numbers were *Streptococcus faecalis* and *Salmonella infantis.*

Stool specimens of the persons affected contained large numbers of *S. faecalis.* Stools of two of the patients were positive for *S. infantis.*

The contamination of ham with *S. infantis* is noted because of its rarity, and the data available indicate the outbreak was due to either a mixed infection of enterococci and salmonellae or to *S. infantis* alone.

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Published concurrently with this issue:

PUBLIC HEALTH MONOGRAPH No. 64 . . . Family Group Therapy. *John Elderkin Bell*

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SYNOPSES

MADDOCK, DARRELL R. (Public Health Service), SEDLAK, VINCENT A., and SCHOOF, H. F.: ***Preliminary tests with DDVP vapor for aircraft disinsection. Public Health Reports, Vol. 76, September 1961, pp. 777–780.***

Studies in Miami, Fla., using commercial planes, have shown that DDVP vapor, dispensed by an experimental vaporizer into the ventilating system of the aircraft, can produce effective kills of test houseflies distributed at various sites and elevations in the passenger compartment. Air concentrations in the general range of 0.3 μg. of DDVP per liter of air were highly effective.

McDONALD, GLEN W. (Public Health Service), REMEIN, QUENTIN R., and DURDICK, EDWARD J.: ***Results of diabetes screening activities, fiscal year 1959. Public Health Reports, Vol. 76, September 1961, pp. 825–831.***

A total of 177,000 persons were screened for diabetes in community programs in the United States during the fiscal year ending June 30, 1959, according to reports from agencies conducting diabetes screening. From among 7,000 persons screening positive (4 percent of those tested) 4,000 were referred to physicians for diagnosis, on the basis of abnormal screening or retest findings. Approximately 1,100 cases of previously unknown diabetes were discovered.

Blood specimens were tested in practically all programs. In programs testing more than half of the total persons screened, blood tests were considered positive at blood sugar levels of 130 mg./100 ml. or less.

In programs with followup the overall yield was 6.9 previously unknown cases of diabetes per 1,000 persons screened. Yields in the programs differed widely because of variations in populations tested and in testing techniques. A comparison of this overall yield with prevalence estimates of 8.0 cases of unrecognized diabetes per 1,000 population demonstrates the need for increased case-finding efficiency in diabetes screening programs. Greater yields would result from direction of screening programs toward known high-prevalence groups, such as persons over 40 years of age, relatives of diabetics, the obese, and parents of large babies. Yields are also improved by more sensitive screening methods and greater followup efforts.

DICKMAN, ALBERT (Dickman Laboratories, Philadelphia): ***Experience with VDRL flocculation antigen in the Kolmer complement fixation test. Public Health Reports, Vol. 76, September 1961, pp. 832–836.***

All too frequently, in the millions of serologic tests for syphilis performed annually on presumably healthy individuals, reactive laboratory findings are obtained which are not supported by clinical findings. In the Dickman Laboratories among "problem specimens" submitted for the TPI test, of 796 reactive by VDRL slide tests 54.6 percent were negative by TPI test. Of 724 reactive cardiolipin Kolmer tests 385, or 53.2 percent, were negative by the TPI test. There is no relationship between degree of reactivity of the Kolmer test and VDRL slide tests and TPI results.

With serums submitted primarily for premarital examination, reactive Kolmer tests in the presence of nonreactive VDRL slide tests were generally negative by the TPI test. Of 86 such specimens 82 were negative by TPI. Although a 1:150 antigen dilution is recommended in the Kolmer test, a 1:320 dilution seems to be optimum. VDRL flocculation antigen, when used in a test dose of 0.5 ml. of a 1:320 dilution in the standard Kolmer procedure, has a high degree of sensitivity. Compared with the standard Kolmer test, the complement fixation test employing VDRL antigen gives fewer confusing weak reactions in presumably negative serums from a group with a low incidence of syphilis.

The use of VDRL antigen as a complement fixation antigen might be profitably evaluated in a future Serology Evaluation Research Assembly study.

The Mental and Physical Health of Students of Nursing

HERMAN E. HILLEBOE, M.D.

A YOUNG WOMAN who selects nursing as a career picks more than a profession; she chooses a way of life. As a nurse she will learn to think her way into patients' feelings. Her outlook will be one that combines professional requirements with deep regard for human values.

Her work will require her to develop the personal resources she will need to give comfort and help to the sick in their time of need. By constantly giving to others she will insure her personal growth as a human being.

If our nurses are to perform at their effective best someone must insure that they have the chance to enjoy good physical and mental health. Where they live, work, and spend their leisure hours has everything to do with their health. The Helene Fuld Health Foundation is a bright example of what can be done to provide these surroundings for nurses.

Good medical care can do much to decrease illness and time lost among student and graduate nurses. A thorough program contains four essentials: (*a*) readily available health services of high quality; (*b*) a healthful working environment; (*c*) work schedules that do not continually overtax physical and emotional resources; and (*d*) adequate housing and recreational facilities.

Health Services

The first health service a student of nursing benefits from is a thorough medical examination. It is a prerequisite to the physician's total planning for her and to her responsibility for her own health throughout her school life and later.

The young woman who applies for entrance to a school of nursing has outgrown the pediatrician but not the sensitivity to all childhood infections. She is subject to diseases such as mononucleosis, gastroenteritis, appendicitis, and acne. She may have experienced some of the gynecologic problems of young womanhood. She may possess the mixed-up drives, feelings, and the anxieties and exhilarations that characterize many of her age group (*1*). There will be few other times in her life when a careful, intelligent appraisal of her mental well-being by a sympathetic physician and a friendly conference with him will pay better dividends.

The initial history and physical examination offer a candidate for nursing school an opportunity to obtain professional help in evaluating her health practices. The advice she receives may one day help her avert or postpone the onset of clinical illness (*2*).

The medical examination should be thorough, but it should also be a pleasant educational experience. Carefully asked questions in taking the candidate's history can elicit hidden fears, aggressions, hostilities, and frustrations (*3*).

Some nursing schools ask that the candidate's family physician send a transcript of her health and family history to the examining physician of the school prior to the first examination (*4*). This saves the school physician

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Dr. Hilleboe, commissioner, New York State Department of Health, presented the first Helene Fuld Lecture at Trenton, N.J., May 26, 1960, under the auspices of the Helene Fuld Health Foundation, which has as one of its major interests the health of students of nursing.

from asking routine questions about family members, childhood diseases, and injuries. It is also useful to have the candidate fill out a health questionnaire before she appears for her examination. Either technique allows the physician to devote more time to health guidance during the candidate's initial visit.

Some nursing schools cannot provide their students with a full array of specialist services to augment those of the internist or general physician, although many schools do so by calling on community resources.

One school associated with a large general hospital follows an effective plan which begins with the applicant's family physician. With her application papers, each candidate is sent two forms to be filled out by her family physician. One is the Pre-entrance Medical Record recommended by the National League for Nursing; the other is an immunization form prepared by the school health committee. On the latter form, the physician records immunizations for smallpox, diphtheria, tetanus, typhoid fever, and poliomyelitis, and results of the Wassermann test. The school health adviser, who is a member of the admissions committee, reviews the completed forms and notes any irregularities that the applicant may present. He then suggests that minor difficulties be corrected before the candidate is admitted to the school.

During orientation week, the health adviser discusses with each student her responsibilities for maintaining good health. He explains the procedure for physical examinations, the importance of immunizations against communicable diseases, the facilities of the student health service, the school health insurance plan, and the value of good health habits.

A few weeks later the student of nursing undergoes a complete medical examination by the school physician. This includes a physical examination, a urinalysis, a hemoglobin test, a tuberculin test, a chest X-ray, and a dental examination. Her height, weight, blood pressure, temperature, pulse, and respiration are recorded and the record is placed on file in the school health service. The health adviser compiles the family and individual health histories. These records, together with laboratory reports, X-ray films, and results of other examinations, comprise the student's health record.

The school physician then reviews the results of her laboratory tests and medical reports with each student. He observes her posture and examines her feet. A podiatrist recommends proper types of shoes and checks these before they are worn. This is an important part of the examination and is too often overlooked in the health appraisal of persons who are on their feet most of their working day.

If further examinations are needed, the student is referred to the appropriate specialist.

Continuous Followup

What happens after the nursing student's initial medical examination is as important as what precedes it. Immunization booster schedules should be scrupulously followed. Any occurrence of diarrhea should lead to a search for enteric pathogens. The student should be queried about staphylococcal infections and asked to report any new infections promptly. This will help to avoid spreading an insidious invader through the newborn nursery and the surgery unit. The student should also be watched for allergic reactions, for she is being exposed for the first time to an enormous number of biological products, chemicals, new acquaintances, and new surroundings.

At annual examinations or in group discussions on health with the school physician or nurse instructor, it is desirable to teach students how to make self-examination of the breasts for early evidence of tumors. This examination should be made monthly throughout life. Later, in her professional career, the nurse can teach the procedure to her female patients.

At least once a year a history should be taken and a physical examination given each student. Several schools of nursing schedule three examinations for junior and senior students: one before they begin their clinical experience, another at the end of their junior year, and a final one at the end of their senior year.

Medical Care

Whenever possible, one person should have full responsibility for the general health service for students of nursing (*5*). Medical care should be readily available so that students will feel free to ask advice whenever they fall ill or notice symptoms of illness. Here a student

learns firsthand the full meaning of the physician-patient relationship and of the insights into health that this brings.

In some centers, there is a tendency to belittle nurses' complaints on the ground that psychosomatic ailments are common among students of medicine and nursing. Psychosomatic complaints, however, may be indications of severe emotional stress and, unless these are relieved by sympathetic medical counseling, and therapy when indicated, they can interfere seriously with the academic and clinical progress of a student, cause her needless mental anguish, and, in some cases, prompt her to use palliative forms of self-treatment that can be uselessly expensive or openly harmful. All complaints should be heard sympathetically and their ultimate significance understood by the student. Complaints may indicate illness for which diagnosis and treatment should not be delayed. Early diagnosis is as important for a student's own health as it is in the advice she gives to potential patients and their families.

To prevent the spread of disease, students who come down with "colds," minor respiratory ailments, and pyogenic infections should report to the health service physician promptly. Clinical and classroom instructors should see that students with colds and other infectious ailments are isolated and receive adequate medical attention (*6*). One or two days of bed rest for an acute cold will frequently save needless loss of time by avoiding complications. Rest in bed will also prevent infections from spreading to other students and to staff members and thus avoid further loss of time.

Sick Leave

If medical care is made easily available and no penalties are levied for time lost to illness, much can be done to encourage students of nursing to guard their health. Some hospitals enforce strict rules about absences from classes or from clinical practice, requiring students to make up time lost because of absenteeism. Rules of this sort are patently unsound because they make students unwilling to take time off to seek medical attention.

The school which allows a realistic amount of sick leave follows a wise policy and ultimately will reduce the amount of illness among its students and other personnel. Two weeks of sick leave a year is reasonable, and the time could well be cumulative throughout the school years.

Payment for Medical Care

The question of payment for medical care is important. If too heavy financial responsibility is placed upon students and their families, students in modest financial circumstances may avoid seeking care. Some schools provide free medical services through the staffs of the hospital with which the schools are associated. In other schools, group health insurance for students of nursing is common and a good practice for nurses to continue after graduation.

Counseling Services

It takes self-appraisal and self-discipline to acquire the warmth and serenity of the professional nurse who has had a balanced education of mind and body, but it can be done if students have the understanding help of teachers and medical advisers. There is no better time in life to attack mental and emotional problems than in the postadolescent years of the student. Early attention to emotional and social problems will help her build up a reservoir of mental stability, a working insight into the personalities of patients and co-workers, and an understanding-in-depth of her own drives and problems.

Included among the human relationships which students establish may be the all-important ones of marriage and motherhood. Sympathetic counseling has great value at such times of decision and adjustment.

For the overweight student whose obesity is a manifestation of a deep emotional problem, psychological counseling is the only course of treatment that is fair to both student and school and which has any chance of continuing success. Few things are more difficult for a heavy person to achieve than a permanent loss of weight, and no overweight student should be placed on a reducing diet until someone has tried to determine the cause of her obesity.

Students caring for tuberculosis patients in a tuberculosis hospital should have chest films taken 3 months before and from 6 weeks to 6 months after the planned experience. Students receiving BCG vaccine may require more fre-

quent chest films during periods on tuberculosis services because the tuberculin test usually becomes positive after vaccination and no longer serves as an indicator of fresh infection.

The health department suggests a tuberculin test for students who have undergone heavy exposure to tuberculosis and who have not had BCG vaccination. If the tuberculin test is negative, it should be repeated every 3 months for 18 months. If the test converts from negative to positive, a chest X-ray should be taken and repeated every 3 to 6 months for 18 to 24 months. Many experts advise giving converters prophylactic doses of antituberculosis drugs for 1 year. This decision can best be made by a consulting chest specialist.

Known tuberculin reactors who are exposed to active tuberculosis should have chest X-rays within 4 to 6 weeks following exposure and every 3 to 6 months thereafter. The length of followup should be based upon the advice of the supervising physician.

The New York State Department of Health also recommends that the chest health status of each student be evaluated upon graduation and that she be given a systematic protection plan to follow during her professional years.

Protection Against Tuberculosis

Most hospitals in which students of nursing obtain clinical experience take routine chest X-rays of all patients on admission, so there is little likelihood that any student will be unknowingly exposed to tuberculosis. However, in those hospitals which do not take chest films of all new patients and in hospitals with tuberculosis services, students with negative tuberculin reactions should be considered candidates for BCG vaccination.

Students feel that the practice of taking chest X-rays at the beginning and end of each hospital affiliation is unnecessary and undesirable. Exchange of X-ray films among hospitals and judicious use of tuberculin tests would give the hospital and the students the protection they need and would keep the number of chest X-rays at a minimum.

The New York State Department of Health recommends the following procedures for the protection of students of nursing against tuberculosis:

- An initial chest X-ray film of each student on admission to the school of nursing and one every 12 months thereafter.
- Tuberculin tests of nonreactors to tuberculin at regular intervals between X-ray examinations.
- A cooperative arrangement whereby hospitals with which nurses affiliate will accept either a chest film or its reading.

Protection Against Radiation Hazards

In many hospitals, exposure to any form of ionizing radiation is a real hazard for nurses, and it will increase in importance in this age of new X-ray techniques, use of radioactive isotopes in diagnosis, and use of intensive radiotherapy. Nurses who accompany patients for fluoroscopic and X-ray examinations are exposed to definite hazards. For example, it is common practice for nurses to hold infants during X-ray examinations. When this is unavoidable, the nurse should have the same lead shielding as the radiologist.

In the department of radiology at Johns Hopkins Hospital in Baltimore, nurses are not allowed in the radiation therapy rooms, and only under rare circumstances are they permitted in the diagnostic rooms (personal communication from Dr. Russell H. Morgan). When they must be present for a diagnostic procedure, they wear the kind of lead aprons and gloves worn by fluoroscopists. Special care is taken that they do not expose themselves to the direct beam of the X-ray tube. A technician from the radiation safety office computes the safe distance from each patient who is given isotopes or radium, and nurses maintain a position beyond this distance and keep direct contacts with the patient to a minimum. In general, pregnant nurses are not assigned for experience on floors where radioisotopes are in use. This protects both the mother and the highly radiosensitive tissues of the fetus, especially during the early months of pregnancy.

Environment for Healthful Living

Healthful living, in its deepest sense, calls for harmony of physical, intellectual, and emotional resources. Therefore, living quarters, social and recreational programs, vacations, the environment and scheduling of learning and

work, some of which spell creative leisure, are of the utmost importance to students of nursing.

Living Quarters

Some students in schools of nursing live at home, some live in other quarters of their choice, and some in dormitories with students in other schools. Most students live in residences provided by the school. Students' residences separate from the hospital are desirable. They should provide for the health and safety of each occupant and should offer wholesome living quarters and study rooms. A fire-resistant structure is the best protection against fire. An adequate number of exits and accessible firefighting equipment are a necessity, as is knowledge of each occupant's role in case of fire.

A single sleeping room for each student is desirable, and for students assigned to evening and night experience, a single room is imperative. Double rooms should have ample closet space and a set of basic furnishings for each occupant—bed, dresser, desk, reading light, desk chair, bookcase, and comfortable chair. Lighting should be tested by modern methods and students should learn its relation to sight conservation. For the comfort of the second occupant, lights should be adequately shielded.

In dormitories, bath and toilet units should be in a ratio of one unit to not more than six, and preferably four, persons. A dressing booth should be located outside each shower. Handwashing bowls in each bedroom are desirable. If they are not provided, the ratio in the central unit should be one bowl for every three persons. Every central toilet room should have a handwashing bowl even though there is one in each student's bedroom. Space and equipment should be provided for laundering personal things, for sewing, and for cleaning garments.

An informal lounge area with an adjoining kitchen and dinette is desirable for each floor of the students' quarters. Some arrangements should be made for recreation, depending of course upon the size of the residence. Reception rooms for guests, both men and women, are highly important, and coat rooms and lavatories should be provided for guests. The residence should be attractive and friendly in atmosphere. Color and decoration should be pleasing. Home is for rest, study, creative leisure, quiet thought, companionship, and fun.

Social and Recreational Programs

The nursing profession makes greater physical and emotional demands on women than almost any other calling. For this reason, an organized program of social and recreational activities is imperative. If a student is to learn to perform at her peak, she must have leisure activities that provide relaxation, physical exercise, and a change in the faces around her.

Although a young woman should be able to plan for most of her own time, the school has responsibility for organizing basic social activities. Well-planned activities sponsored by the school can be a satisfying focus of social life for students of nursing. Such activities not only refresh and relax, but give a new perspective to a young woman who may be away from home for the first time.

Dividends accrue to the school and to the hospital in which the student practices nursing when the social program seems to say to students, "You belong here and we're glad to help you round off the sharp edges of life into something more pleasant." Such a program gives the young student the feeling of well-being that accompanies a sense of belonging. A feeling that she belongs to something worthwhile is a source of inner strength to her in times of new experience and of crisis which come often for nurses. Loyalty to a school and a hospital, and appreciation of its solicitude, can be a blessing to students and can return continuing benefits to both.

Exercise and Nutrition

Sports and other physical activities should be encouraged the year around. Some provision can always be made for both outdoor and indoor exercises (*7*). Outdoor tennis courts, indoor swimming pools, and gymnasiums are standard equipment at some nursing schools. If the school does not have these facilities, arrangements for their use can oftentimes be made elsewhere in the community.

One school has adapted a course of the university's department of physical education to the needs of student nurses (*8*). The purpose

of the course is to develop the motor skills of students, to prevent physical strain, and to help them conserve time and energy in their personal and professional activities.

The course consists largely of practical application of the general principles of body control. Through discussion and practice, students learn to apply the physical laws of movement to everyday activities and to movements used in nursing and in sports.

The course teaches students how to relax, how to improve their coordination, and how to minimize fatigue-producing tension. Under the guidance of a discussion leader, they work out for themselves the most effective methods of stooping, bending, lifting, pulling, and pushing, and discover the reasons the methods are effective.

The food served both student and graduate nurses should not only be appetizing, wholesome, and sufficient in quantity, but it should be prepared attractively and served in pleasant surroundings. Too often the hospital dining room is a noisy, bustling place where the students and staff eat drab, unimaginative food to the cacophony of clanking dishes, the blare of the public address system, inevitable shop talk, and hospital odors. Under these circumstances, it is small wonder that many students bolt their food or eat at a lunch counter around the corner.

Quiet attractiveness should accompany all meals and opportunities for greater attention to the amenities of dining, interesting conversation, relaxation, and change should accompany special meals which are scheduled frequently.

Environment of Clinical Experience

The environment of students of nursing during their periods of clinical experience is more important than most people realize. Factors such as inadequate physical facilities, improperly functioning equipment, lax methods of housekeeping, sanitation, and asepsis, and chronic shortages of hospital supplies and personnel bear cogently upon the health of students who are learning and practicing the care of patients (*9*). Accidents due to faulty equipment and poorly planned facilities cause serious loss of time and result in needless disabilities among personnel.

The general sanitation of a hospital affects not only the health of students and of employees, but the effectiveness of its teaching programs as well. If the hospital staff does not practice what its nursing instructors preach, the hospital can hardly expect its students to acquire good nursing habits. It will do a nursing instructor little good to preach use of handwashing techniques in the classroom if staff nurses habitually fail to practice them in the nursery or if facilities are not available.

Staphylococcal infection rates among hospital patients are good indexes of breaks in sterile techniques as well as in soap-and-water cleanliness. Reports of a series of outbreaks in the United States and abroad indicate that in many hospitals staphylococcal infection rates approach 15 percent. However, some hospitals have been able to lower their infection rates to as low as 1 percent. Understaffing makes breaches in aseptic technique easy and also encourages nurses to ignore their own small infections.

Daily and Weekly Schedules

There are wide differences among schools in their educational philosophy and planning. Some plan tight and full schedules of instruction and clinical experience. In some of these schools, there is heavy concentration of science courses in the first term, long hours of clinical practice, and frequent assignments to night and evening experience throughout the program. Time schedules are rigidly adhered to. Comment on the quality of such education is inappropriate here, but the demands it makes on health and the lack of opportunities it affords for personal development are appropriate considerations for those concerned with the emotional and physical health of students and for regulation of schedules in relation to health throughout the program.

Other schools balance and interrelate science and clinical learnings, eliminate unnecessary repetition in practice and, through dynamic teaching, elicit high motivation for learning and self-direction from the students. Schedules are flexible. The health programs in such schools have high potential value for the students' learning, as well as for their health.

In some schools, students are permitted to work in hospitals or elsewhere in order to earn needed money. These students should have special health surveillance.

Some schools operate on the basis of academic years with vacations during summer, at major holidays, and between terms. Other schools adhere to hospital schedules for holidays and weekends. An annual vacation of at least one month is recommended for these schools.

Summary

A dynamic health program provides services in keeping with the best medical practices in diagnosis, therapy, prevention, and the achievement of positive physical and mental health. These services are provided in such a way as to encourage students to use them freely, naturally, and as part of their education for a health profession. The program is concerned also with the health elements of the environment of study, clinical experiences, daily living, and recreation. These elements can be molded to guide students into professional and personal enrichment.

A dynamic health program for students of nursing benefits the many people nurses care for throughout their lifetimes. It enhances the attractions of nursing as a profession. It moves youth toward self-fulfillment and enriches their gifts to humankind.

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Resources for Environmental Health

An Office of Resource Development (Environmental Health) has been established in the Bureau of State Services, Public Health Service. It will be the Bureau's central office for study and development of resources in the field of environmental health, particularly in air and water pollution, radiological health, occupational health, and environmental engineering and food protection. The office will coordinate the work of the various divisions of the Bureau in administering research grants, fellowships, and training programs and in developing research facilities. Studies of manpower in environmental health will also be conducted by the office. Frank A. Butrico has been selected to head the office.

A branch to administer grants for training or research has been established in the following divisions of the Bureau of State Services: Air Pollution, Environmental Engineering and Food Protection, Occupational Health, Radiological Health, and Water Supply and Pollution Control.

Toledo's Well-Oldster Conference

A report of the first year of the Well-Oldster Conference in Toledo, Ohio, has been prepared by Dr. Hilbert Mark, Dr. C. J. A. Paule, Hazel Deuble, and Helen Day, all of the Toledo City Health Department. The conference, started in March 1959, is a 5-year project developed by the health department in collaboration with the Academy of Medicine of Toledo and Lucas County.

The basic purpose is to develop a standard medical approach in evaluating the health of presumably healthy older persons. This entailed development of a history form; testing selected screening techniques as practical methods of casefinding among the aged; determining the normal ranges in laboratory tests for older persons; demonstrating the value of periodic health appraisals for the aged; finding ways to motivate older persons to seek regular examinations; developing an effective pattern of referrals from the appraising staff to private physicians, dentists, and clinics; establishing the optimum period between appraisals; determining the effectiveness of the cooperation that can be achieved between the health department, medical society, and individual practitioners and clinics.

The 119 "well-oldsters" initially admitted were recruited through the cooperation of senior citizens clubs and newspaper, television, and radio announcements. Some were referred by private physicians and clinics.

To enroll in the program, the only requirements are that the person be aged 65 years or over and presumably in good health. After registration, enrollees are given appointments for their first health appraisal and orientation to the program.

The appraisal requires three visits to the clinic. It comprises analysis of the blood for serologic reactions, cholesterol level, glucose, and urea nitrogen; a complete blood count; the Diagnex Blue test for gastroenteric morbidity; urinalysis; chest X-ray; electrocardiogram; vision testing with the Snellen chart; hearing tests; oral and dental inspection; and a complete physical examination including tonometry, sigmoidoscopic examination, and exfoliative cytology. In addition, the patient fills out a Cornell Medical Index (a health questionnaire) and a 3-day dietary intake form; has an interview with a social worker who records information about the patient's personal history, personality, and motivation; and gives his medical history to a public health nurse.

Because the staff found that the Cornell Index and the interviews that were originally relied upon to assess personality were unsatisfactory for research and for tabulation purposes, the 16 Personality Factor Questionnaire, devised by Dr. Eugene Byrd of the University of Miami, was adopted.

Some of the observations made of the medical and laboratory procedures used during the first year were: tonometry revealed several instances of increased intraocular pressure; a more effective enema than soap suds or plain water is needed for proper evacuation before sigmoidoscopic examination for this group (two other types of enema are being tried); serologic tests for syphilis produced only a few positives, of low titer; and exfoliative cytologic examinations showed normal estrogenic levels for most of those examined.

All persons found through appraisals to have conditions requiring medical care were discharged from the conference and referred to a private physician or clinic. Of the 119 persons enrolled, 34 were discharged for medical reasons and 6 for various nonmedical reasons. Hypertension (nine cases) and diabetes (seven cases) were the most frequent causes of medical discharges. As patients are dropped from the conference, new ones are admitted from a waiting list.

Those retained receive their second health appraisals 6 months after their first. Between appraisals, they attend a series of seven classes on nutrition, recreation, general and mental hygiene, dental health, care of the feet, and home safety.

During the first year of operation, 42 of 85 persons retained from the first appraisal had been in the project long enough to receive a second one. Of these, eight failed to report for their appointments. Of the 34 who did report, 5 were discharged for medical reasons.

Subsequent appraisals will continue to be held at 6-month intervals. As with the first appraisals, the findings of the subsequent ones are reviewed and recorded on McBee cards. The conference staff will publish a progress report after 3 years.

Waterborne Infectious Hepatitis Epidemic From a Chlorinated Municipal Supply

DAVID C. POSKANZER, M.D., and WILLIAM G. BEADENKOPF, M.D.

IN DECEMBER 1956 the bureau of epidemiology and communicable disease control of the New York State Department of Health was informed that a number of cases of jaundice had occurred in the township of Rhinebeck, N.Y. Preliminary investigation suggested that transmission of infection might have occurred through the chlorinated municipal water supply. Although spread of hepatitis by chlorinated water systems has been reported twice before (*1*, *2*), additional documentation of an outbreak presumably caused in this manner seems indicated.

Within Rhinebeck Township lies the incorporated village of Rhinebeck, with an estimated population of 2,300, situated about 2 miles from the Hudson River. Along the river in the same township and connected to Rhinebeck by a road is a smaller community, Rhinecliff, with a population of 660 (fig. 1).

The two communities are served by three physicians, Dr. Martin J. Poppo, Dr. William G. Thompson, and Dr. Frederick C. Cohn. All three cooperated in the study. These physicians live in Rhinebeck and practice in a wide surrounding rural area. They stated that, prior to the present episode, they could recall only rare cases of jaundice, and these were, in their opinion, obstructive rather than infectious.

Dr. Poskanzer is with the department of neurology, Massachusetts General Hospital, Boston, and Dr. Beadenkopf is director of the heart disease epidemiology section, New York State Department of Health, Albany. At the time of the study Dr. Poskanzer was an officer of the Epidemic Intelligence Service, Communicable Disease Center, Public Health Service, assigned to the New York State Department of Health, and Dr. Beadenkopf was assistant director, bureau of epidemiology and communicable disease control, New York State Department of Health.

Methods

Patients with cases of jaundice reported by the physicians and by the nurses of Rhinebeck Central Schools were interviewed shortly after illness occurred. The interviews were conducted by medical students under the supervision of the authors. Inquiry was made about clinical symptoms, illness in other members of the household, milk supply, water supply, sources of food, contact with other persons who had had jaundice, public gatherings attended, meals taken outside the home, and exposure to hepatotoxins and inoculations. Only clinical jaundice was accepted in defining a case for epidemiologic analysis. While this criterion excluded a few reported cases, the exclusion would not be expected to obscure the mode of spread of the infection. It was impractical in this outbreak to attempt to locate and diagnose persons with nonicteric hepatitis who were not under medical care.

In order to determine whether reporting by physicians and by the school nurses had revealed most of the jaundiced cases in the area, additional inquiry was made by means of a community survey. Seventeen members of the class of 1957 of Albany Medical College visited every fifth house in the village and surrounding rural area. Visits were made to 57 households in all.

Results

The first case of infectious hepatitis with jaundice was reported on November 21, 1956.

Within 30 days, 70 cases had been reported, 41 in females and 29 in males. The community survey failed to uncover any additional cases not previously reported. In all, 83 cases were reported during the epidemic.

In most instances, the illness described began with anorexia, fever, and malaise, followed by nausea, vomiting, excretion of dark urine, and the development of jaundice. With the onset of jaundice, general improvement occurred. About 20 patients were hospitalized, usually for short periods, but in general the disease was mild. Conjunctivitis, hematuria, and aseptic meningitis were not encountered, and none of 12 blood examinations showed leukocytosis. No preceding wave of gastroenteritis was observed, such as has been reported in several other hepatitis outbreaks considered to be waterborne (*3–6*).

Gamma globulin supplied by the American National Red Cross through the State department of health or obtained through commercial sources was used extensively by the physicians for treating family contacts. The families of all patients with reported cases of jaundice received this prophylaxis. This may have limited the number of jaundiced cases. Two cases occurred in each of three families. Intervals between first and second cases were 3, 13, and 15 days, respectively, indicating that the cases were probably co-primary. In these second cases in three families, one patient had received no gamma globulin, one received it the day after onset of symptoms, the third received it 11 days prior to onset.

Age distribution of infectious hepatitis with jaundice, Rhinebeck Township, N.Y.,[1] 1956–57

Ages (years)	Cases through—					
	Dec. 7, 1956[2]		Dec. 19, 1956[3]		Feb. 1, 1957[4]	
	Number	Percent	Number	Percent	Number	Percent
0–4	0	0	1	1.4	1	1.2
5–14	9	22.5	[5] 22	31.4	27	32.5
15–24	6	15.0	10	14.3	11	13.3
25–34	13	32.5	[6] 16	22.9	18	21.7
35–44	5	12.5	10	14.3	12	14.5
45–54	5	12.5	6	8.5	7	8.4
55–64	0	0	0	0	0	0
65 and over	2	5.0	5	7.2	7	8.4
Total	40	100.0	70	100.0	83	100.0

[1] Including Rhinecliff and village of Rhinebeck.
[2] 17 days after onset of initial case.
[3] 30 days after onset of initial case.
[4] 72 days after onset of initial case.
[5] 1 patient resided within village water supply limits, but used well water.
[6] 1 patient resided outside village water supply limits.

Age and Residence

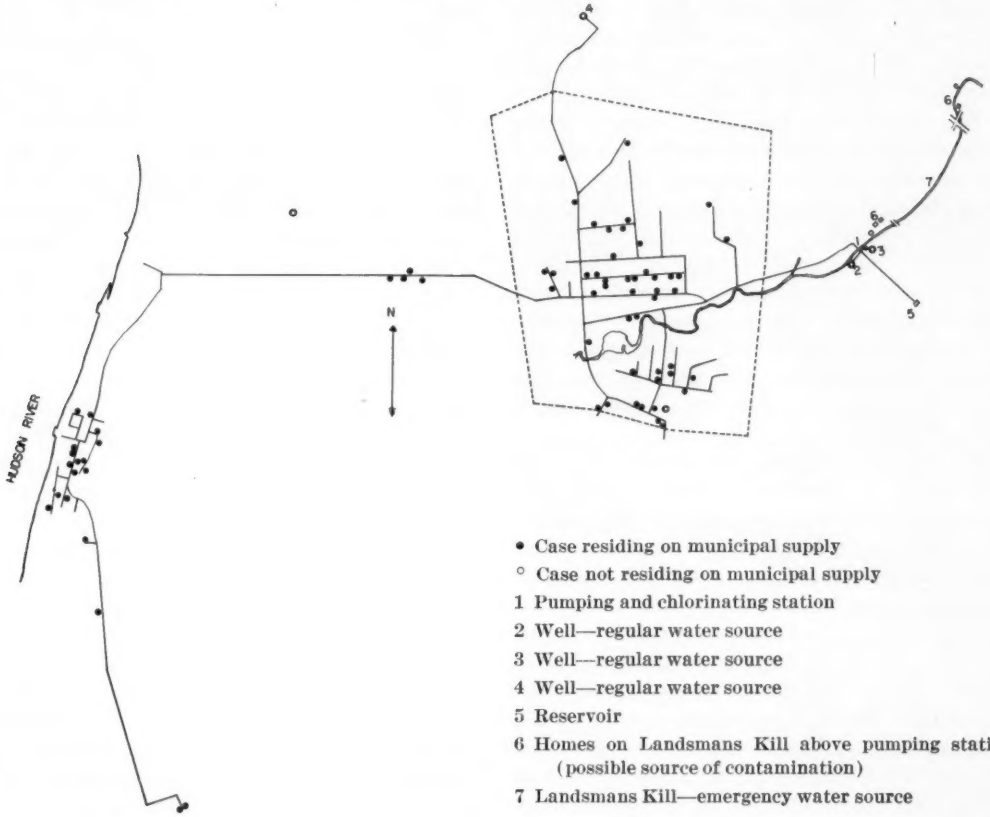
The age distribution of the patients is given in the table. The initial cases were not school centered. A tabulation of age distributions through December 7, 17 days from the initial case, shows the largest number of cases at this stage to be in the 25- to 34-year age group. However, the highest proportion of cases in the epidemic as a whole occurred in the 5- to 14-year age group, a finding consistent with the usual age distribution of cases reported in other epidemics of infectious hepatitis in New York State. Only one case was reported in the age group under 5 years, possibly because the disease in younger children tends to be milder and without clinical jaundice.

Twenty-nine of the first 70 cases reported were in children attending the Rhinebeck Central Schools. Only one of these children resided off the village water supply, although half the children attending the schools resided outside the village and off the village supply.

Half the school children live within walking distance of the schools and half live in an area which extends 16 miles east, 6 miles south, 3 miles north, and to the river on the west. The school district encompasses all of the township of Rhinebeck and substantial portions of four adjacent townships. The children are divided between an elementary school (kindergarten through fourth grade) in the center of the village and a larger school on the outskirts (grades 5 through 12). Nine cases of jaundice were reported among 394 students in the elementary school, while 20 cases occurred among the 500 students attending the upper school. Two additional cases were reported from a military academy on the outskirts of Rhinecliff, the last station on the water supply.

After the first few cases were noted, the illness rapidly became the major topic of con-

Figure 1. Water system of village of Rhinebeck and Rhinecliff, N.Y., and location of 70 cases of infectious hepatitis with jaundice occurring in the first 30 days of the epidemic, 1956–57



- • Case residing on municipal supply
- ° Case not residing on municipal supply
- 1 Pumping and chlorinating station
- 2 Well—regular water source
- 3 Well—regular water source
- 4 Well—regular water source
- 5 Reservoir
- 6 Homes on Landsmans Kill above pumping station (possible source of contamination)
- 7 Landsmans Kill—emergency water source

versation in the village, and cases which might not ordinarily have been seen by physicians came to their attention. Children who lived outside the village, but attended school in Rhinebeck would have been seen immediately by a physician or a school nurse had they become jaundiced.

Possible Modes of Spread

Milk. The milk supply of the families in which cases of hepatitis occurred came from four different commercial dairies. In four families the milk was either evaporated, dried, or fresh unpasteurized.

Food. Family food supplies came from at least 12 different stores, including 3 large chain markets. Five families purchased most of their food outside Rhinebeck.

Insects. The epidemic occurred in December so that flies and mosquitoes were not considered to be important possible carriers.

Contact. Seven churches and a dozen restaurants were mentioned by various families. No history of a common meeting place other than at school over the 2 months preceding the outbreak could be elicited. As is indicated above, the age distribution of patients with early cases of hepatitis is not consistent with a contact-spread school-centered epidemic (*7*).

Hepatotoxins and injections. No unusual incidence of insecticide spraying or general use of chemicals or medications was found. Histories of injections were largely limited to poliomyelitis vaccine in children. These were given in the offices of all three physicians who serve the community.

Water. The water supply of Rhinebeck and Rhinecliff normally is obtained from three

wells; two are situated to the east of the village, a third to the north. In recent years, however, this water supply has become inadequate in the summer, and an emergency unapproved supply has been taken from Landsmans Kill which flows through the village close to two of the wells (fig. 1). Attempts to dig additional wells were unsuccessful through the fall of 1956, and the emergency water supply was continued to meet the demand. This supply was subjected to chlorination, but not to other water purification techniques. The water from the two wells close to the pumping station was chlorinated. The third well, to the north of the village, was sealed, was in good condition, and though not chlorinated, had been found to be free of bacteriological contamination.

Records of the water chlorination plant for the month of November 1956 revealed that residual free chlorine levels tested daily ranged from 0.35 ppm to 0.6 ppm by the orthotolidine test using the "flash" method. The orthotolidine test used in this fashion is said to be inferior to the orthotolidine-arsenite determination (*8*), but it is adequate if read within 15 seconds of the addition of orthotolidine to the specimens. There is no significant manganese in the water supply which might interfere with the validity of this determination. The New York State Department of Health recommends a minimum concentration of free residual chlorine for a disinfecting period of at least 10 minutes ranging from 0.2 ppm at a pH of 6.0 to 0.8 ppm at a pH of 10.0. These levels had been achieved at Rhinebeck, according to plant records.

Samples of water taken on December 12, 1956, a month after probable contamination of the supply of the two communities, revealed a coliform count of 15 MPN per 100 ml. at one sink tap in a greenhouse in Rhinecliff. (MPN indicates the most probable number of coliform organisms and is a standard determination based on a statistical analysis of the laboratory procedure.) Other specimens taken at the same time from scattered taps in the village, however, showed counts of less than 2.2 MPN. The significance of this one contaminated specimen cannot be ascertained, but no other specimen taken from the supply in the year preceding or 6 months following has shown a coliform count greater than 2.2 MPN per 100 ml.

Coliform counts are taken from four to six taps on the municipal supply each month. Specimens of raw water taken from Landsmans Kill above the intake of the chlorinating system have shown coliform counts from 240 to 930 MPN and indicate gross contamination of the raw water supply. Though no cases of infectious hepatitis were located in dwellings close by the stream above the intake point, the supply could readily have been contaminated by these dwellings which emptied their cesspool overflow into the stream.

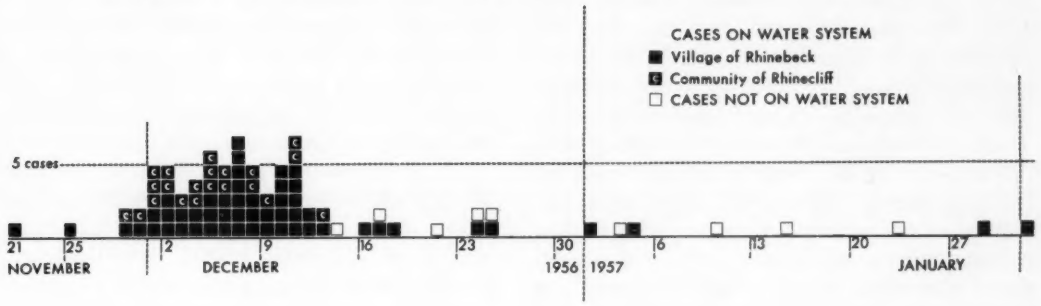
Discussion

The course of the hepatitis epidemic as illustrated in figure 2 appears to be consistent with a common source epidemic. The majority of the cases occurred within a period of time shorter than the recognized incubation period of infectious hepatitis. Few of the cases could therefore be considered secondary. In addition, the rise and fall of the epidemic curve itself suggests a common source of infection.

Though separated by 2 miles, Rhinebeck and Rhinecliff share a common water supply. The geographic distribution of cases, separated into two groups 2 miles apart, but connected by a common water supply, argues for the water supply acting as a common source of infection. It was first thought that the occurrence of two cases in students at a military academy mitigated against the waterborne hypothesis until it was found that the academy is the last drawing point on the village water supply.

When the 70 cases of infectious hepatitis occurring in the first 30 days of the epidemic were plotted on the spot map (fig. 1), it appeared that all but two of the individuals involved in the epidemic resided in houses on the municipal water supply and that the remaining population of the township, estimated at 1,400 individuals, was almost uninvolved. One of the two patients not on the water supply resided within the village but claimed to drink only well water; the other did not live on the municipal waterlines. Radial spread of the disease could not be demonstrated.

Figure 2. Infectious hepatitis with jaundice, Rhinebeck Township, 1956–57



Thirteen cases occurred in the township from December 21 through February 1, a period of nearly a month and a half following the first 30-day wave of the epidemic. Six cases were located on the municipal water system and seven were not (fig. 2). Only four cases were reported in the ensuing 6-month period.

Twenty-one of the 57 families interviewed in the community survey drank well water exclusively. Five families claimed that they boiled their water because they suspected that the water supply was contaminated. Thirty-one of the families interviewed drank municipal water. No previously unreported cases were discovered in these interviews.

It is interesting to speculate about the actual instance of contamination of the water supply. The first wave of 70 cases occurring within 30 days of the first case, or within the generally accepted incubation period for infectious hepatitis, can be readily separated from the cases which followed (fig. 2). If a common source is assumed for these 70 cases, then the midpoint of the epidemic curve for these cases is December 7. A mean incubation period of 25 days would indicate that contamination occurred about November 11 (Sunday). The first 70 cases had onset from 14 to 37 days from that date. Contamination of the water supply on a day when children were not in school could account for the absence of cases in children who attend the school but reside off the water system.

It might be inferred from the epidemic curve that contamination occurred in only one instance or over a short period. Rain may have increased the amount of organic matter in the stream over a short period, thus temporarily protecting the virus present in the water from the action of the chlorine, or the water may actually have been contaminated in only one instance with feces containing virus. It is also possible that chlorination was inadequate on a single day and that the insufficiency was not determined by the test for chlorine levels as recorded.

Epidemics of infectious hepatitis, presumably waterborne, had been described by a number of authors (*3, 4, 9–12*) prior to the classic work of Neefe and Stokes (*13*), who demonstrated the transmission of the infection from a contaminated well and through water from the well to human volunteers. The largest number of such epidemics have been reported as a result of contamination of ground water supplies—both wells (*10–20*) and springs (*3, 6*). Contaminated surface water supplies have also accounted for several epidemics: one involving a contaminated river supply where the purification and chlorination plant was not functioning (*4*), three due to contaminated streams (*9, 21, 22*), and one due to a contaminated lake supply (*5*). Rabe (*23*) and Warren (*24*) observed small epidemics which appear to have been borne through large disrupted municipal water supplies. In both instances, definite contamination with *Escherichia coli* was demonstrated frequently. The literature concerning waterborne infectious hepatitis has recently been thoroughly reviewed by Mosley (*25*).

The work of Neefe and his associates (*26, 27*) demonstrated through human volunteer studies that the normal treatment of municipal water supplies may be inadequate to inactivate the hepatitis virus. They showed that inactivation was complete with free residual chlorine levels of 1.1 and 0.4 ppm after 30 minutes con-

tact in coagulated, settled, and filtered water, but that 1.08 ppm total residual chlorine after 30 minutes contact did not inactivate the virus in otherwise untreated water, as indicated by infection of two of five volunteers who drank it. The observation is similar to that reported by Trask, Melnick, and Wenner (*28*) working with poliomyelitis virus. They found that when extraneous organic matter was added to a suspension of poliomyelitis virus, though sufficient chlorine was added to meet the additional demand presented by the organic matter, the chlorine level then had to be further increased 10 to 18 times to inactivate the amount of virus in the original suspension. These authors pointed out that the inactivation of a virus in a water supply contaminated with organic matter is a very different problem from the inactivation in a laboratory.

Only three epidemics of hepatitis have been reported in connection with water supplies known to be chlorinated. The epidemic reported by Hayward (*29*) of at least 52 cases occurring in a Pennsylvania city of 60,000 might be explained on the basis of transmission by the water supply, but the evidence is inconclusive and the epidemic may have been contact spread. Sundell (*1*) reported a common-source epidemic from a lake supply which was filtered and chlorinated. The water was bacteria free after treatment. Of the 391 cases reported, 32 percent of the patients were icteric. The author felt that the number of nonjaundiced cases was greater than usually encountered because the virus was attenuated by partial chlorination. Originally 0.8 mg. of chlorine per liter was added to the water supply. This was later increased to 1.2 mg. per liter, but the epidemic continued. When the chlorine level was raised to a level of 0.4 mg. of free chlorine per liter, corresponding to total chlorine added of 6 mg. per liter, seven times the original amount of chlorine used, and the contact time increased to 60 minutes, the epidemic ceased within 30 days.

Perhaps the most spectacular epidemic is that of 29,000 cases in the city of Delhi, India, in 1955–56, described by Melnick (*2*) and Viswanathan (*30*). Because of a shift in the bed of the river from which the water supply was drawn, "the people of New Delhi were drinking half river water and half sewage from November 13 to November 17." Though the water is subjected to accepted procedures of settlement, coagulation, filtration, and disinfection in modern plants before it is delivered to Delhi consumers, additional amounts of chlorine were added to the water to secure adequate levels when the presence of gross sewage in the intake was noted. However, at least 29,000 cases of infectious hepatitis occurred in the community served by this water supply, even though by bacteriological analysis the efforts to increase disinfection were successful. It is interesting that no increase in the gastroenteritides including typhoid fever, was reported.

Summary

An epidemic of 83 cases of infectious hepatitis with jaundice occurred in two neighboring New York State communities between November 21, 1956, and February 1, 1957. Seventy of the cases occurred within the first 30 days of the epidemic. The two communities, although 2 miles apart, had a common water supply. As an emergency measure water was taken from a stream potentially subject to pollution. It was chlorinated but not otherwise treated. Only 2 of the first 70 patients did not reside on the water supply. The distribution in time of the cases is consistent with a common-source epidemic. Milk, food, contact, insects, hepatotoxins, and parenteral inoculations appeared very unlikely as common sources of infection. It is concluded that the epidemic of infectious hepatitis was waterborne through the emergency water supply, despite the fact that the water was chlorinated.

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Public Health Service Research Highlights in 1960

The following items were taken from "Research Highlights, National Institutes of Health," presented to the Congress of the United States.

A survey of cancer in New York State for 1949–51 found that incidence was generally higher in urban than in rural populations. The urban-rural ratio was higher for males than for females. The incidence pattern was in substantial agreement with those for Connecticut and Iowa (p. 11).

Scientists in more than 150 hospitals in the United States and Western Europe were evaluating 159 drugs in some 200 clinical studies of cancer treatment (p. 20).

In experiments with hamster cells propagated in tissue culture the vast majority of cells surviving sublethal doses of X-rays repaired radiation damage before division and did not transmit damage to daughter cells. Cells underwent repeated cycles of damage and repair with no apparent weakening of the repair process (p. 32).

Eastern encephalitis virus was isolated from the *Aedes vexans* mosquito for the first time by Yale scientists. Less than 5 percent of the specimens collected were of the *Aedes vexans* species, but the only virus isolation was made from members of that species (p. 107).

Monkey malaria was transmitted by mosquitoes to two workers in an NIH laboratory in Memphis, Tenn. The accidental infections have caused investigators to plan reexamination of the entire question of host-specificity of primate malarias (p. 116).

Studies of rheumatic fever cases found that patients who eventually suffer from rheumatic heart disease usually show heart valve damage during their first attack of rheumatic fever, and that patients whose first attack does not produce valve damage usually remain free from rheumatic heart disease, even after subsequent attacks (p. 82).

Preliminary work with a fluorescent antibody technique for detecting the malaria parasite in blood smears indicated that the method, when fully developed, may enable technicians to screen many more suspects for malaria in a day than is possible with present methods (p. 118).

Concentrations of sodium pentachlorophenate (NaPCP) as low as 0.05 ppm in the water habitats of *Australorbis glabratus*, a snail vector of schistosomiasis, were found to greatly reduce the fecundity of the snails and to decrease the viability of the eggs produced (p. 121).

The report of a 3-year study designed to determine the possible relationship between high incidence of intestinal parasitism in mental hospital patients and housing facilities stated that greatly improved sanitation had little effect on transmission of intestinal protozoa. There was a small reduction in the incidence of helminthic infection (p. 126).

A timesaving new test, based on tellurite reduction, for differentiating pathogenic staphylococci from harmless strains was developed in Salt Lake City and reported in the *Journal of Laboratory and Clinical Medicine*. Isolates are streaked on a tellurite-glycine agar plate; after overnight incubation, pathogenic isolates show jet black colonies indicative of growth with reduction of tellurite (p. 134).

The value of a diet low in the amino acid phenylalanine in preventing or delaying severe mental deficiency from phenylketonuria (PKU) was established. PKU victims are unable to convert phenylalanine into tyrosine, resulting in abnormal accumulations of it in the blood. A child's IQ drops 5 points every 10 weeks after birth that the diet is delayed. A relatively simple diagnostic blood test for PKU was developed in 1959 at NIH (p. 161).

A pilot project for screening infants for phenylketonuria, galactosuria, and other forms of aminoaciduria that may cause mental retardation was begun in Cincinnati. Squares of filter paper are given to mothers of newly born children. The paper is placed in diapers when the babies are 4 to 6 weeks old. The dried squares are returned to the hospital, where the urine is analyzed (p. 259).

A simple and rapid test was found for detecting children who may develop Wilson's disease (progressively fatal degeneration of the liver caused by abnormal copper metabolism). The test measures the amount of the plasma copper protein, ceruloplasmin, in the blood. Early detection is important since symptoms rarely occur before age 7, although the metabolic defect is present from birth. If latent disease is found, measures can be taken to minimize absorption of copper from the diet and to promote excretion of copper already absorbed (p. 163).

A long-term study established that the caries-preventing effect of taking daily a fluoride tablet (containing 2.21 mg. of NaF) is comparable to the effect of drinking fluoridated water. However, the investigators concluded that the method is not as practical as water fluoridation (p. 209).

The findings of a long-term study intended to uncover the causes of alcoholism were reported in *Origin of Alcoholism* (Stanford University Press). A group of 225 boys selected in the 1930's were traced to adulthood. Of these, 29 became alcoholics. By statistical comparison, the investigators found traits that typified alcoholics even in childhood. The alcoholic subjects had undergone a variety of frustrating experiences; they were more likely to have suffered neurological disorders and more likely to have come from a home disrupted by severe conflict and basic disagreement (p. 264).

The R. E. Dyer Lecture

Epidemiologic Models in Studies of Vector-Borne Diseases

GEORGE MACDONALD, M.D.

THE CENTER of interest and point of emphasis of any living subject changes. The center of active interest in epidemiology gravitates to the United States of America, and I pay homage to the outstanding quality and volume of work I have seen in this country. It is therefore a unique privilege to give the Dyer Lecture at the National Institutes of Health, and especially to do so in the presence of Dr. Rolla E. Dyer, who is largely responsible for the stature of the Institutes and after whom the lecture is named.

An epidemiologic model is a closely argued statement of the quantitative aspects of transmission of a disease. This model includes all those factors with a direct influence on the dynamics of transmission and shows proportionately, but not necessarily in exact numerical terms, how changes in any one or all of the factors will influence transmission, incidence, and prevalence.

The model taken by itself has no significance; it proves nothing and explains nothing, except perhaps the mind of the man who made it. Its value lies in its potential use as a tool for understanding the patterns in which the disease occurs, the causes of divergence between them and of fluctuations in prevalence, the relative significance of individual factors and of changes in their values, for checking biological knowledge, and for analyzing its completeness for epidemiologic purposes.

Study of malarial infections was originated by Farr (*1*, *2*), who successfully fitted a smoothed curve on a smallpox epidemic and later predicted the probable future course of an epidemic of rinderpest on the basis of a mathematical examination of past happenings. This method of predicting the course of infections was elaborated in relation to direct infections by Brownlee (*3*), Hamer (*4*), and others, and by Ross (*5*, *6*) in relation to infections conveyed by an intermediate host, the mosquito. From about this time, 1906, an active literature on the subject flourished, culminating in the monumental work of Lotka (*7*), but the subject then went into a state of suspended animation, with very little literature after that date until after World War II, largely because the models produced had not in fact served as useful tools in the understanding of natural happenings. Notably the theoretical models of direct infections showed a small but consistent difference from natural epidemic curves, while those of malaria required, to simulate nature, the attribution of values to constants which no malariologist would accept as realistic.

The study of both types of infection has since been revived, and realistic models of direct and indirect infections are now produced.

Dr. Macdonald, director, Ross Institute of Tropical Hygiene, London, England, delivered this lecture November 15, 1960, at the National Institutes of Health, Public Health Service.

In the case of direct infections it has been shown that deterministic models such as were developed by earlier workers are not properly applicable to the transmission of infections in communities which are subdivided into innumerable cells by the facts of housing and town life, whereas stochastic models can be appropriately developed for them. In the case of the indirect infections it has now been realized that some of the basic definitions on which earlier workers relied were inaccurate; their correction makes possible the production of realistic models, which have been elaborated in relation to malaria (*8–12*). Moreover, the deterministic technique remains applicable to many cases of these infections, perhaps because their dissemination by migrating insects blurs the barriers to transmission from house to house. The use of these definitions has thrown much light on the epidemiology of malaria. Particularly they have shown the existence of true epidemiologic patterns in what had previously been an endless series of widely varying pictures, and they have demonstrated the relative importance of changes of value in the various factors influencing the extremely complicated chain of transmission. I now consider them an indispensable aid in the understanding of any of the indirect infections.

The methods involved in the mathematical analysis are not abstruse, and the technique is well within the mathematical power of many biologists. The difficulty of the subject to a biologist lies in directing his thoughts into the wholly quantitative channels of dynamics, in lack of acquaintance with the type of steps involved in building up a complete model, and in the lack of apparent meaning in the ultimate product of some previous studies which have been left in their mathematical form without back translation into biological terms. To the biometrician they present no technical problems whatever; his difficulties lie in recognizing the needs of the epidemiologist and the type of analysis which might be helpful to him.

My present lecture is an exercise in translation, an effort to explain what steps may be helpful in creating a model, what factors need to be taken into account in each model, how the models integrate with one another, and the type of information which may be derived from them. I will use malaria for demonstration of these steps, but I hope to show that the principles can be applied to other conditions, and what type of modification is necessary to do so. The process falls into three stages, each of which may have a number of subdivisions: (*a*) the formulation of a general scheme showing what factors are directly involved in the dynamics of transmission; (*b*) the arrangement of one's ideas to form such combinations of these factors as are logical and germane to the subject, and (*c*) the examination of the steps of transmission, first as a series of isolated events, and then as a working mechanism in which the movement of one cog affects another, and so to form a complete picture.

A biological picture has to be converted into quantitative terms to form the general scheme. Figure 1 illustrates the transmission cycle of malaria. Within the circle the cycle is shown in traditional form, from schizonts through gametogenesis, fertilization, sporogony, inoculation into man, and the exo-erythrocytic cycle back to schizogony. Outside the circle are the quantitative aspects of these happenings. Infection in man has the characteristics of duration and infectivity, both of which can be expressed numerically. The infective patient is bitten by mosquitoes which have the characteristics of numbers, frequency of biting man, susceptibility to malaria, and longevity; the sporogony cycle has the characteristic of time, which may be used to subdivide the mosquito's pattern into a probability of survival to infectivity, and subsequent expectation of life should it do so. Sporozoite-infected mosquitoes have a certain average infectivity, though it

Figure 1

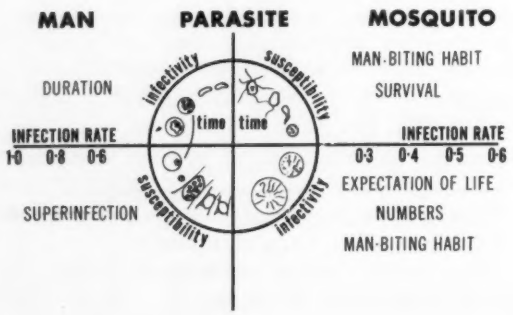
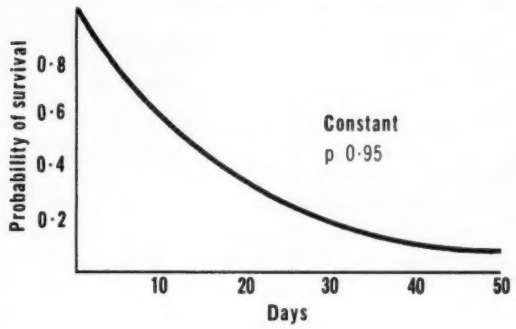


Figure 2. Survivors from a constant mortality rate



Identities

Probability of survival to n days	p^n
Expectation of life	$\frac{1}{-\log_e p}$
Number of feeds on man	$\frac{a}{-\log_e p}$

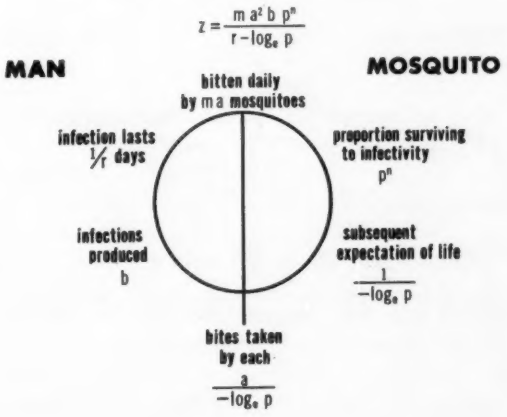
Where a is average daily feeds

can be measured only in conjunction with the susceptibility of man. Finally, a characteristic of new infection in man is that it can often be superimposed on a previous infection. The interaction of these characteristics produces ultimately one infection rate in man and another in the mosquito. It will be convenient in several later diagrams to adhere to the general form used in this one, because it visually relates a given infection rate in man on the left, through the upper semicircles, to one in the mosquito on the right, and the infection rate in the mosquito through the lower semicircle to a rate in man again.

The second step is the formation of appropriate combinations, or derivatives, of these basic factors. One such set of derivatives is shown in figure 2. It is a reasonable, though not exact, representation of natural happenings to consider the mortality of anophelines as unrelated to age. On this basis it is possible to express for any given probability of survival through 1 day (p) the probability of survival for any given number of days, such as the time of sporogony (n), and the expectation of life of a mosquito from any age at which it is known to be alive. A combination of this expectation of life with the probability of biting man on any one day (a) gives the total number of bites on man taken by the average mosquito during its whole lifetime, the great significance of which is brought out in mathematical working and which therefore deserves a title for easy reference. It may be termed the "total biting figure."

Another important combination is the basic reproduction rate, or number of infections which would be distributed by a single patient with a primary case of malaria if no infections were blocked by previous infection of mosquito or man. The concept, illustrated in figure 3, is quite simple. If the probability of recovery on any day, or the recovery rate, is r, the duration of infectivity is $1/r$ day. The patient with the primary case is bitten on each of these days by ma mosquitoes, m being their numbers in relation to man and a being the probability of their biting man on any one day. The probability of their survival to infectivity (p^n), and the number of subsequent feeds on man by those which survive for this period $\left(\frac{a}{-\log_e p}\right)$ can be derived from figure 2. A proportion (b) of these feeds will actually implant infection. Simple multiplication of these gives the basic reproduction rate. This is a concept only, many of these infections in nature being blocked by previous infection of the mosquito or man. Its full justification lies in the fact that expressions worked with fully rigorous allowance for the basic reproduction rate can often be simplified

Figure 3. The basic reproduction rate



by substitution of this identity, which is adequate proof of its value as a concept.

The third step is to examine the dynamics of transmission, and for this there are needed:

- An expression for the dependence of the mosquito infection rate on a constant inoculation rate in man.
- The converse expression for the dependence of the human infection rate on a constant inoculation rate.
- An expression for the way in which these rates mutually adjust to each other when both are free to change, an increase in one causing a corresponding rise in the other and so ad infinitum, though in progressively smaller stages till virtual equilibrium is reached, which the expression should represent.
- Some expression or representation of the sensitivity of this equilibrium to changes in its controlling factors.

Figure 4

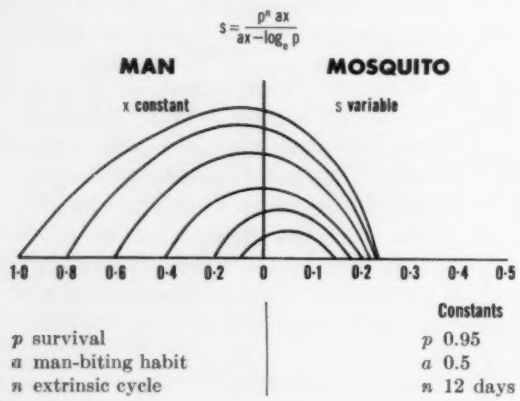


Figure 5

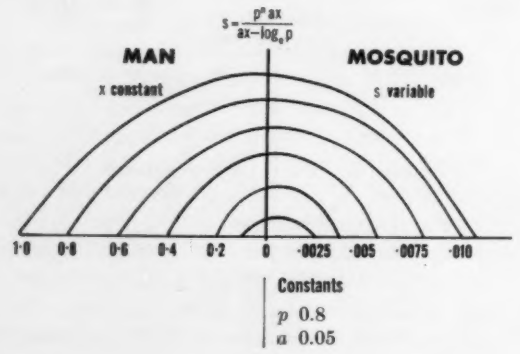
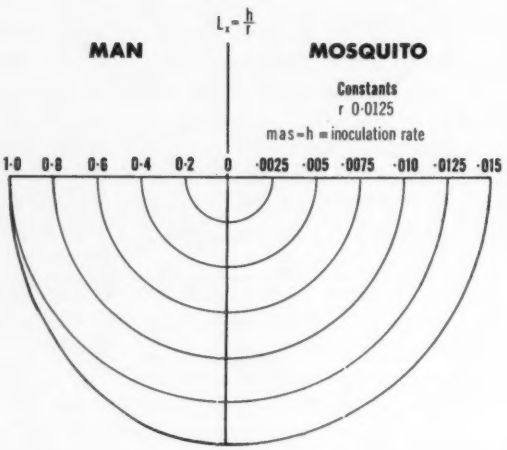


Figure 6



These expressions will, so far as appropriate, be illustrated by two contrasting examples, in one of which the anopheline carrier is given a high total biting figure, and in the other a low one.

Figures 4 and 5 illustrate the effect of a constant human infection rate (x) on the mosquito infection rate (s), the symbols p, a, and n having the meanings given previously. The ruling expression, derived from Macdonald (*10*), is given at the head of the figures. Figure 4 shows the relationship when the total biting figure is high, 9.25, being determined by high values of both the biting habit and longevity, such as are typical of *Anopheles gambiae*. An increasing human infection rate causes a disproportionately small increase in the mosquito infection rate; or a high total biting figure restricts the correspondence between the two infection rates. Figure 5 refers to happenings when the total biting figure is low, 0.224, being determined by low values of both biting habit and longevity, such as are characteristic of *Anopheles culicifacies* in parts of India. The actual values of the mosquito infection rate are much lower than in the previous example and are shown on a different scale, but in this case an increase in the human infection rate is matched by an almost exactly proportionate increase in the mosquito infection rate; a low total biting figure permits almost complete correspondence between the two infection rates.

The inoculation rate (h) depends on the in-

fection rate in mosquitoes (s), their numbers (m), and the frequency with which they bite man (a). If all of these are constant, and allowed to operate for sufficient time, during which immunity is not enhanced, the resultant human infection rate will gravitate toward a limiting value (L_x) in which the only other component is the recovery rate (r), and this limiting value is in direct proportion to the value of the inoculation rate until infection is general (fig. 6). This simple form differs from that seen in most infections. It is decided by the fact that superinfection occurs, and the method of its mathematical handling was shown by Irwin in a paper by Macdonald (8).

If both the infection and inoculation rates are variable, an increase in one causes a corresponding increase in the other, and so on indefinitely, but in steadily decreasing degree, till the two rates approach a limiting value, shown in the expressions at the head of figure 7, which itself is diagrammatic only. The possible range of the human infection rate extends from 0 to 1.0, and that of the mosquito infection rate from zero to p^n. The full expressions for the limits are lengthy, but it is possible to simplify them to the forms shown by insertion of the identity for the basic reproduction rate. The human infection rate is determined by the total biting figure, which occurs in a reciprocal form, and the reproduction rate. The mosquito infection rate is determined by the reproduction rate and the probability of survival to infectivity (p^n). It will be noted that, if the reproduction rate (z) is put at 1.0 or less,

Figure 7. Limiting values

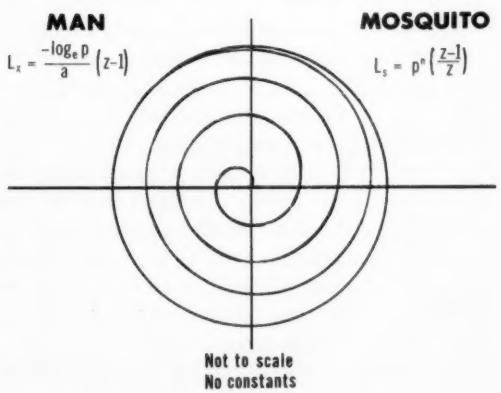


Figure 8

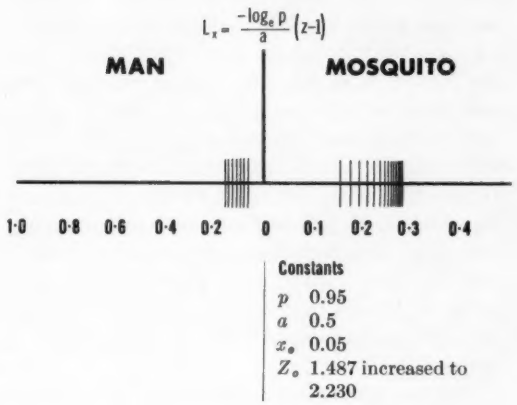
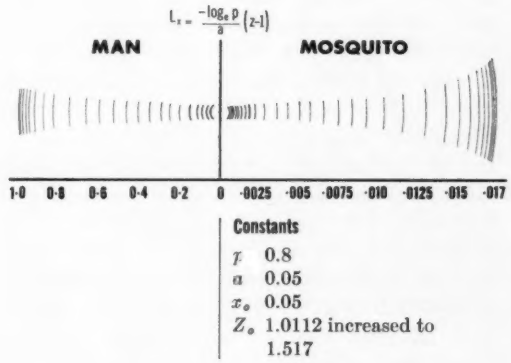


Figure 9



both of the infection rates become 0 or unreal, and this is the basis of the concept of the critical level of transmission, below which the disease disappears, as in anophelism without malaria. With long-standing transmission the basic reproduction rate would itself undergo change, on account of the reduction in the duration of infections owing to the development of immunity, and this is the reason for omission of any numerical statement of these expressions in the diagram.

Examination of the concept of these limits can nevertheless be very fruitful. This may best be illustrated by examination of the degree of change in the two limits produced by alteration of the basic reproduction rate. This is shown for the two extreme cases in figures 8 and 9, which are on the same principle as previous diagrams though the connecting links

between the two sides have been eliminated for the sake of simplicity. The first concerns happenings when the total biting figure is high, 9.25, as used in figure 4. It is assumed that the human infection rate had previously been stabilized at 5 percent, and the fact that immunity may have played a part in this is irrelevant. The basic reproduction rate is then assumed to have increased by 50 percent, and the changes in the two infection rates are followed through their successive increases to their new limiting values. In figure 9 the same series of happenings is followed, but the total biting figure involved here is small, 0.224 as in figure 5.

The two sets of happenings are quite distinct from each other. In the first case the two infection rates increase by small steps, the human one gaining stability again at 12.6 percent. In the second, both rates increase by progressively larger steps until saturation is approached, and the human rate does not settle down until it reaches 100 percent. These figures show diagrammatically the working of stability, instability, and equilibrium, for which the full proof lies in complete mathematical working. A high total biting figure results in a stable infection rate which is relatively insensitive to changes in the controlling factors, whereas a low total biting figure determines a very unstable state of equilibrium which is drastically upset by small changes in the transmission. Any of the factors which enter into the reproduction rate may of course determine this change, but the degree of effect on the infection rates is determined solely by the total biting figure.

This picture has been presented in a precise mathematical form elsewhere (*11*), the present statement being an effort to translate it into simpler terminology. It accords well with natural happenings, both as regards variations in the stability of the disease, and association of this variability with anopheline characteristics. Figure 10 shows the endlessly repetitive seasonal malaria of Italy before its eradication, transmitted by *Anopheles labranchiae* which feeds commonly on man and lives long, while figure 11 shows happenings in Ceylon, also before eradication of malaria, where the disease showed haphazard and extreme variation, great

Figure 10

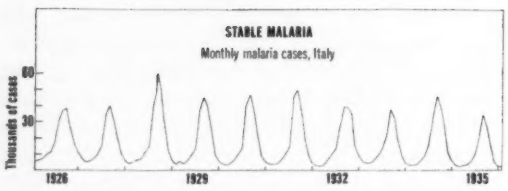
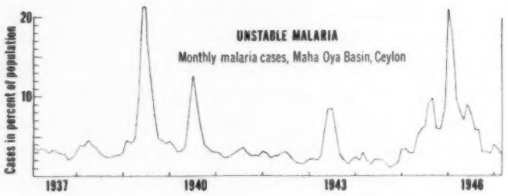


Figure 11



epidemics following minor changes in transmission, under the influence of *A. culicifacies*, which has characteristics of biting and longevity similar to those used in preparing figures 5 and 9.

Examination of a mathematical model can also throw valuable light on the theory and practice of control measures. The effect of control of the breeding is shown in figure 12. Variations in mosquito density produce a directly proportionate change in the reproduction rate, as can be seen by examination of the expression at the head of figure 2. A great reduction in density must therefore be attained if an originally high reproduction rate is to be lowered below the critical level.

However, it may also be seen from the expression at the head of figure 2 that mosquito survival (p), representing differences in expectation of life, enters into the reproduction rate twice, and in a complicated form. Figure 13 shows the effect of changes in this expectation of mosquito life. It is assumed that within a given set of values of mosquito density and biting habit, an expectation of 20 days ($p=0.95$) had sustained a reproduction rate of 1,000—a realistic figure. Reduction of this expectation produces a corresponding decrease in the reproduction rate, but on a vastly greater scale, till when it reaches 2.6 ($p=0.68$) the reproduction rate sinks below its critical level and full control is achieved.

The immense success of imagocidal control

came as a surprise to malariologists, but it is explained and could have been foreseen by examination of models of this sort. It would be wise to examine the theory of controlling other diseases, to search for the most effective techniques and not merely allow their possible development by chance.

To what other mosquito-borne infections can this model be applied? None. But its mechanism can be modified and adjusted, with appropriate parallel biological criticism and study, to give comparable information about any other, and I briefly examine the forms of change which would be needed for application to filarial and virus disease transmission.

The scheme of filarial disease transmission differs in that it often kills the mosquito, in which the infective stage lasts for only a short period, so that a different expression is needed for the dependence of the mosquito infection rate on that in man. So far as present biological knowledge goes, the dependence of the human infection rate on the mosquito infection is in identical form with that of malaria, controlled principally by the occurrence of superinfection. However, in the series of data which I have examined there has been a great discrepancy between the apparent inoculation rate shown by entomological study and the effective rate deduced from the age incidence of infection in man, the one being several hundred times as high as the other. The cause might be either that the biological picture inserted is wrong, or

Figure 12. Mosquito density and reproduction rate

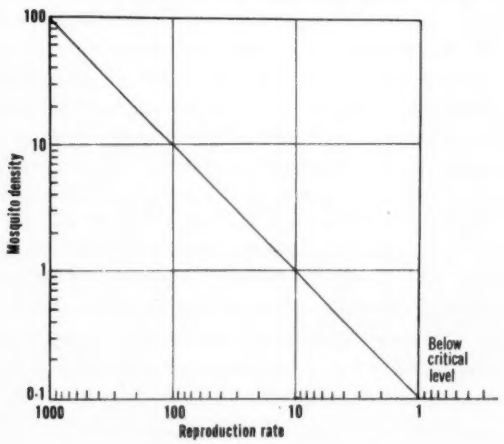
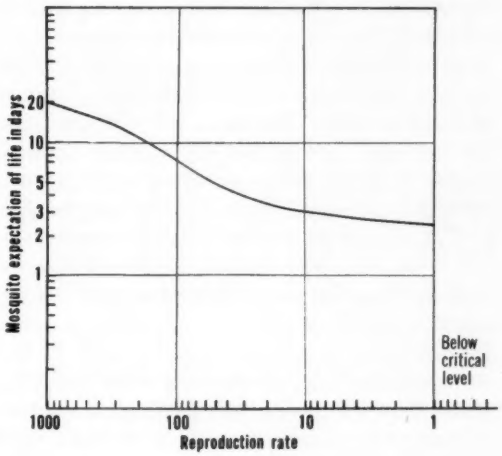


Figure 13. Mosquito expectation of life and reproduction rates



that an extremely low value should be attributed to the infectivity factor, termed "b" in the malarial equation. I have not seen this commented on in the literature and feel some exploration of this subject is essential to the reliability of models of filarial infection.

Since coming to the United States I have been impressed by the interest in mosquito-borne virus infections and have tentatively explored the production of an appropriate model, outlined in the section "Mathematical Background," but it has been tentative only and applies to a hypothetical condition, the verisimilitude of which would require a considerable check. The general scheme of dependence of the mosquito infection rate on the rate in vertebrates is identical, the same considerations apply, an incubation period is involved, and the infection, which does not kill the insect, lasts for the remainder of its life. The scheme of dependence of the infection rate in vertebrates on the infection rate in the mosquito is, however, radically different. Superinfection does not occur; neither in my hypothetical case does reinfection, though it could readily be allowed for. The infection may kill a significant proportion of those infected, and the high immunity developed restricts the possibility of new infections, the frequency of which is closely influenced by the proportion of new nonimmune arrivals, by birth or other means, who

must be taken into account. Some of the main features of such a model are:

- The limiting value of x, which represents the total of immune and infected persons, is in a quite different form. It is invariably below 1.0, and has a very indirect relationship to the inoculation rate. The total biting figure does not enter into it; this figure has some minor influence, but mainly on the speed at which the limit is approached, and less on its actual value.
- The model shows the relationship which exists, when stability is achieved, between viremia, immunity, and mosquito infection, and the significant way in which this relationship is dependent on migration and birth rates.
- The sensitivity of the total rate, including those immune, is relatively slight, but the sensitivity of the viremia rate is high, the degree of variation following changes in any of the controlling factors being partly determined by the migration and birth rates.
- The model indicates the critical levels of transmission, and the way in which the critical density of mosquito vectors is influenced by, among other things, the total biting figure.

This statement, if its scheme were approved by those working in the subject, refers only to the equilibrium levels, though there would be no peculiar difficulty in preparing epidemic pictures. It could therefore be applied in its present form in places only where equilibrium may occur, characteristically in the perennially warm tropics. It is put forward only to indicate the possible utility of mathematical models in such conditions, not as a definitive structure. It is probable that such an approach might remove some of the mystification which now accompanies discussion of the epidemiology of these conditions, as well as throw light on some factors deserving study, such as the frequency with which birds are bitten by mosquitoes and their migration and birth rates.

Malaria and arborvirus infections are broadly similar in that they are both mosquito-borne. A very brief statement of preliminary studies of schistosomiasis will illustrate the value of this type of study in a condition where the vector carriage has essential dissimilarities.

The biological cycle of transmission of schistosomiasis, shown diagrammatically within the circle in figure 14, is well known. The worm

Figure 14

in the vertebrate host passes eggs, from which miracidia hatch in water as free-living organisms. If the miracidia come into contact with a suitable snail they may penetrate it and develop through a complicated cycle of multiplication, which ends in the discharge of cercariae. These are again free living until they come into contact with a vertebrate, in which they develop to adult worms, if it is of the correct species. There is a very considerable body of knowledge of the dynamics of parts of this cycle in the vertebrate and in the snail, and of the snail itself. This has not, however, cleared up considerable mystification about the epidemiology of the disease or about its control.

Few imagine that universal eradication of host snails is possible, or that contamination of water can be totally prevented, and any widely applicable scheme of prevention will probably include elements of control of contamination, snail density, perhaps snail viability, and contact of man with natural waters. No one knows, however, the relative efficiency of these measures except that each would be effective if pushed to absolute efficiency. The formation of a model could throw light on the uncertainties of both epidemiology and control.

The first essays in modelmaking immediately emphasize the inadequacy of considering the transmission cycle in two halves, as is usually unconsciously attempted, in man and in the

snail. Progress is impossible unless it is made in four stages: the dynamics of happenings in man, in the first free-living aquatic stage, in the snail, and in the second aquatic stage. The essential governing factors in each of these stages are shown in the figure, within the circle so far as they are attributes of the nematode alone and outside it when they are partly or wholly characters of the medium.

Logically the first step is to assume a constant rate of contamination of water with miracidia and to examine the factors which convert this into an inoculation rate of the snails which it contains. The logical and mathematical process is simple and results in the expression

$$h=\frac{kc}{1+ks}$$

where h is the probability that a snail will be penetrated by a miracidium in unit time, or rate,

c is the number of miracidia liberated in unit volume of water in unit time, or contamination rate,

s is the number of snails present in unit volume of water, and

k is constant representing the probability that one miracidium, liberated in unit volume of water in which there is a single snail, will succeed in penetrating it, or scanning power.

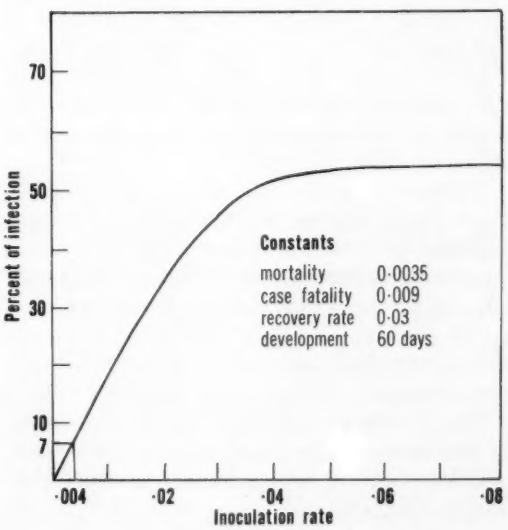
The influence of changes in the contamination rate can be readily derived from the expression. The inoculation rate varies directly with it. However, the influence of changes in snail density cannot be derived without some knowledge of the scanning power. At some initial densities it is great, at others small, but since the literature contains no traceable reference to measurement of scanning power we have no conception of even its order of magnitude and cannot therefore even guess the densities concerned.

This equation is crucial in the dynamics of transmission of disease, and it might be said that the model had failed to throw light on the subject. This is not the case. The model does not fail; it represents the truth. The fact that we are completely ignorant of even the order of value of one of the constants involved is no fault of the model, which demonstrates the gap and thereby indicates one line of study which would contribute to a knowledge of epidemiology.

Although a full understanding of the dynamics of schistosomiasis is blocked by weaknesses of understanding such as this, the subject can be pursued to a study of the relationships between the inoculation rate, as it is determined by the factors described above, and the resultant infection rate in snails. Two general types of relationship are to be expected, one in those conditions where the snail population undergoes seasonal regeneration, so that one age group will predominate at any time, and the other in conditions where the population remains undisturbed by seasonal factors and has an age distribution determined only by mortality rates. Allowance must be made for superinfection, for possible recovery from infection, and also for the fact that infection may sometimes prove lethal to the snail. This last has been suggested to have an important bearing on infection rates, and must therefore be taken into rigorous account in the model.

Expressions for these two relationships, which are very complicated owing to the need to take account of lethality continuing during infection, are given in the section "Mathematical Background," and the expression for the second type of condition is illustrated in figure 15. The constants used are derived from the

Figure 15. Trematode infection rates in snails



work of Pesigan and co-workers (*13*) and refer to *Schistosoma japonicum* infections in *Oncomelania quadrasi*. The infection rate would be expected to rise progressively with an increasing inoculation rate until saturation is reached, which with these constants would be at about 50 percent. The author's findings ranged from 0 to 6.97 percent. Even this highest value corresponds only to a daily inoculation rate of about 0.004, or once in 250 days.

This inoculation rate is extremely low, and since we know that it is directly related to the contamination rate, it is clear that changes in the contamination rate within a very broad range would have a direct effect on the snail infection rate. It is, however, far from clear what would be the effect of altering the numbers of snails short of eradicating them entirely. Reduction in their numbers would to some extent increase the inoculation rate, and hence the snail infection rate, but whether this would be proportional or not cannot be told till at least the order of the values of the constants shown to be important by mathematical models is known.

Conclusion

I hope I have demonstrated the value of models in throwing light on epidemiology and in acting as guides to clarification of thought and to research.

These are only examples. In all vector-borne diseases there are comparable points of mystery and confusion which could be cleared up by the same approach—in Africa trypanosomiasis, in the difference between simian yellow fever in Africa and America, in leishmaniasis, and in a host of others.

I hope I have also shown the ways in which the biologist and the mathematician can come together to produce epidemiological models. This involves cooperation and a very strenuous effort at mutual understanding, as well as translation from biological to mathematical terms, and again from mathematical to biological terms, without which it is not complete.

But if mutual understanding is achieved, a proper study of the dynamics of transmission, which a model represents, can be a most valuable help to epidemiology.

MATHEMATICAL BACKGROUND

Malaria

The expressions used are quoted on the figures. A full statement of them is given in Macdonald (*14*).

Schistosomiasis

Number of Miracidia in Water

The following symbols are used:

- m Number of miracidia present in unit volume of water.
- cdt Number of miracidia freshly liberated in unit volume of water in time dt.
- adt Proportion of miracidia which die in time dt.
- bdt Proportion of miracidia which would be immobilized and removed from circulation by contact with a snail in time dt, if there were one snail in unit volume of water.
- s Number of snails in unit volume of water.

It is apparent that

$$\frac{dm}{dt}=c-m(a+bs) \qquad [1]$$

whence, when conditions are static

$$m=\frac{c}{a+bs} \qquad [2]$$

Inoculation Rate of Snails

- hdt Proportion of snails in which a new infection is established in time dt.

Other symbols as above.

By previous definition the number of miracidia present in unit volume of water is m, and the proportion making contact with a snail is bdt, whence

$$h=mb \qquad [3]$$

The value of m given in [2] may be inserted here to give

$$h=\frac{cb}{a+bs} \qquad [4]$$

It is, however, logical to modify this slightly to read

$$h=\frac{ck}{1+ks} \qquad [5]$$

where

$$k=a/b$$

which brings two natural partners together in the form of a/b, the reciprocal of the probability of a miracidium being removed from circulation by contact with a snail, during the whole of its natural life, if the density of snails were one in unit volume. This is termed the "scanning power."

Infection Rate in Snails

The following additional symbols are required:

- f Proportion of miracidium infections which kill the snail.
- vdt Proportion of snails which die, through other causes than these infections, in time dt.
- gdt Proportion which snails newly hatching in time dt bear to the total snail population.
- rdt Proportion of affected snails which revert to the unaffected state in time dt.
- n Period of time taken for development of an infection to maturity, with cercarial production.
- x Proportion of snails with mature infections. The criterion of infection may be either discharge of cercariae or the detection of cercariae on examination after crushing, though the criterion of affected or unaffected, corresponding to r or the recovery rate, should be adjusted to coincide.
- t Time.
- p Probability of a snail surviving through 1 day.
- e Base of natural logarithms.

It is known that superinfection occurs and it follows that the recovery rate, r, needs modification in the form described by Irwin in a paper by Macdonald (*8*), the effective rate being $(r-h)$ when $r>h$, and 0 when $r<h$.

It is also known that infection is sometimes lethal to the snail, and it has been suggested that this may have a significant bearing on the infection rate among them, provision for which must be included in an analysis to allow examination of this type of belief, though it might later be permissible to exclude it if it were shown to have an insignificant effect. Proper allowance for this involves also taking normal death and birth rates into account and, in consequence, the expressions developed are rather complicated in appearance. It should, however, be possible to use simplified forms for rough purposes when there is no desire to take possible minutiae into reckoning.

The line of argument developed by Ross (*15*), in his section V, applies perfectly to the analysis of the infection rate among snails of a given age. Following this, when $h<r$, let

$$\alpha=\frac{r+f}{2f} \qquad [6]$$

$$\beta^2=\alpha^2-\frac{h}{f} \qquad [7]$$

$$L=\alpha-\beta \qquad [8]$$

$$L'=\alpha+\beta \qquad [9]$$

Then the infection rate at any given age is given by

$$x_t=L\left[1=\frac{L'-L}{L'e^{2f\beta t}-L}\right] \qquad [10]$$

The infection rate in a community of snails, the age distribution of which is determined solely by a continuing death rate and birth rate not subject to seasonal or other such change, has been developed with the generous help of Dr. P. Armitage. The working has not yet been published, but it leads to the following expression

$$x=L\left[e^{-(v+Lf)n}-\frac{v+Lf}{r+Lf-f}e^{-(r+Lf-f)n}\right] \qquad [11]$$

which has been used in the preparation of figure 14. When h exceeds r it should be substituted for r in expressions 6 and 11.

Arborvirus Infections

Arborvirus infection in the vertebrate is assumed to be followed, after an incubation period, by a short period of viremia, during which the individual may die, and then by a period of firm immunity in the survivors. The rates for death, emigration, and immigration are the

same for immune vertebrates as for nonimmune animals which do not contract the infection.

The notation used in the text in connection with malaria is followed, except that

f is the proportion of infections which kill the vertebrate during the viremia stage.
x is the proportion of animals which are immune.
y is the proportion of animals with viremia.
r is the probability of recovery from viremia in unit time.
g is the proportion of animals newly born in unit time with respect to the total population.

The expression for mosquito life, and expectation, is the same as used in the statement of malaria, as is also the reproduction rate, z, bearing in mind that the recovery rate, r, refers to the probability of recovery from viremia.

The mosquito infection rate is given by

$$s=\frac{p^n ay}{ay-\log_e p} \qquad [12]$$

The working of these expressions, which is complicated, is not here stated, but it leads to a definition of the final state, when stability is reached and rates are no longer increasing, though free interplay between the two infection rates has occurred. The value of x, the proportion of the population which is immune, is found by solving a quadratic equation, to do which let

$$\gamma=\frac{(1-f)^2}{f}+\frac{ag}{2\,rzf\,(-\log_e p)} \qquad [13]$$

and

$$\delta^2=\gamma^2+\frac{(1-f)}{f}\,\frac{(z-1)}{z} \qquad [14]$$

when the required limits are given by

$$L_x=-\gamma+\delta \qquad [15]$$

$$L_y=\frac{gL_x}{r\,(1-f)(1-f+fL_x)} \qquad [16]$$

$$L_z=\frac{p^n L_y}{aL_y-\log_e p} \qquad [17]$$

The possibility of maintenance of this endemic state depends on the size of the population, its birth rate, the duration of viremia and the case fatality associated with infection. The critical values of these may be roughly estimated by noting that transmission becomes progressively decreased when the value of y is such that it indicates a fractional number.

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Parainfluenza Viruses in Southern Louisiana

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CERTAIN of the many viruses newly recognized during the past decade have been found to possess properties which justify their inclusion among the myxoviruses. Because their shared properties differ somewhat from those of the traditional myxoviruses, they have been placed together to comprise the parainfluenza group (*1*). Knowledge of their prevalence and association with human illness has emerged from Washington, D.C. (*2–5*), Cincinnati, Ohio (*6*), Toronto, Canada (*7*), California (*8*), and Louisiana (*9,10*).

In the course of attempting virus isolations from 343 infants and children hospitalized in New Orleans between May 1959 and April 1960, 13 hemadsorbing agents were isolated. In addition, serums from 380 other individuals were tested for neutralizing antibodies against four of the parainfluenza viruses.

Materials and Methods

Culture systems. Primary cell cultures were prepared from rhesus monkey kidneys (MK) and human amnion membranes (HAM). Continuous line cultures of HeLa (*11*) and FL human amnion (*12*) cells were also used. For monkey kidney cells, growth media included Hanks balanced salt solution (BSS), containing 0.5 percent lactalbumin hydrolysate and 3 percent calf serum. For the other cell types, growth media included Hanks BSS, 1 percent Eagle's basal medium stock concentrates, and 10 percent or 20 percent calf serum. Prior to use all cultures were washed with BSS and re-fed with a maintenance medium. Eagle's basal medium without serum was used for MK cells. For HAM, FL, and HeLa cells maintenance medium was the same with the addition of tryptose phosphate broth to 15 percent and heat inactivated normal rabbit serum to 5 percent. Penicillin, streptomycin, and mycostatin were in all solutions.

Ten- or eleven-day embryonated hen's eggs were employed, using standard virological techniques.

Viruses. Sendai virus strain D/Sendai/52 (*13*) was received from Dr. Keith Jensen in 1956. Allantoic fluid from two egg passages was used in this work. Strain C243 of hemadsorption virus type 1 (HA1) (*2*), strain C35 of hemadsorption virus type 2 (HA2) (*2*), and the Greer strain of croup associated virus (CA) (*6*) were received from Dr. Robert Chanock. Fluids from monkey kidney cell passages were employed as stock for HA1 and HA2. For CA virus stock, HAM cell passage fluid was used.

Detection of virus. Virus was detected in cultures by the hemadsorption technique of Vogel and Shelokov (*14*), as modified by Chanock and others (*2*).

Infectivity titrations were performed by inoculation of four cultures with each tenfold dilution followed by examination for hemadsorption 4 days later. Cell culture infective dose 50 percent (CID_{50}) was calculated by the method of Reed and Meunch.

Specimens. Specimens for isolation were

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collected, at the time of admission, from 322 of an approximate total of 570 patients hospitalized between June 9 and September 10, 1959, in the Tulane Medical School pediatric service of Charity Hospital. Pediatric house officers were urged to collect specimens from every patient admitted. Since it was generally known that these specimens were for virus isolation, it is likely that greatest effort was made to obtain specimens from those with clinical evidence of virus illness. Most of the 322 patients were admitted because of acute inflammatory disease. According to discharge diagnosis, principal localization of the inflammation was respiratory in 25 percent, enteric in 16 percent, central nervous system in 15 percent, and generalized in 5 percent. Three hundred throat swabs, 294 fecal swabs, and 71 cerebrospinal fluid specimens were tested. Specimens were stored at 4° C., and brought to the laboratory within 24 hours for immediate inoculation or further storage at −20° C.

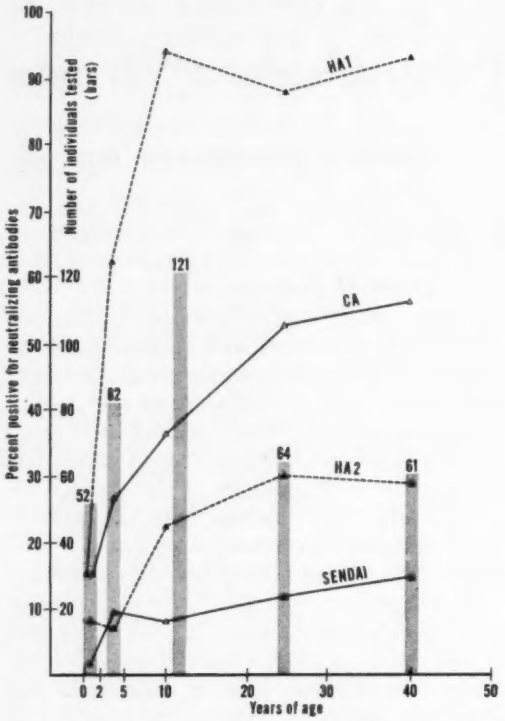
Additional specimens were collected within 24 hours of admission as follows: on May 22, 1959, throat, fecal, and cerebrospinal fluid specimens from a 16-year-old male patient with marked but transient encephalitis, hospitalized at Touro Infirmary in New Orleans; and between December 26 and March 21, 1960, throat swabs from 20 croup patients in Charity Hospital.

All specimens, including cerebrospinal fluid, were collected into 1-ml. aliquots of maintenance medium containing rabbit serum and tryptose phosphate broth.

Human serums were obtained in 1958 and 1959 from residents of New Orleans and two nearby semirural communities to the southwest, during viral ecologic studies directed by Dr. J. P. Fox and Dr. H. M. Gelfand. Serum contributors were members of relatively young, lower socioeconomic families selected because they had young children and were willing to participate. There was fairly even distribution according to sex, color, and residence in New Orleans or the two outlying communities. Serums were stored at −20° C.

Virus isolation. Except for specimens from the 20 croup patients, two cultures of each of the four cell types were inoculated with 0.1-ml. aliquots of a specimen. Incubation was at 37° C. and stationary. Cultures were examined at 7-day intervals for cytopathic effect and finally for hemadsorption at 21 days. When cultures were suspected of being positive for virus effect, second and third passages of the fluid were made to fresh cultures, the third passage providing stock material for the identification procedure. All isolates recognized by their cytopathic effect were tested for hemadsorption. Nearly all the throat specimens were tested in eggs after several months of storage at −20° C. and at least one thawing and refreezing. These attempts were negative and were considered unsatisfactory because of the circumstances of specimen storage.

Percentage of 380 human serums positive for neutralizing antibodies against four parainfluenza viruses, according to age



Specimens from the winter croup patients were inoculated amniotically into embryonated eggs and also into monkey kidney cell cultures. Amniotic fluids were tested for hemagglutination of guinea pig red blood cells after the second of two 3-day passages. Monkey kidney cultures were tested by hemadsorption at 6 days

and, if negative, two additional 6-day passages were made.

Uninoculated control cultures included with each group of primary isolation attempts manifested hemadsorption only in one instance involving FL cultures. There were no positives in the inoculated or other control tubes employed on that day.

Isolate identification. Identification of isolates was attempted by use of antiserums to the four parainfluenza strains studied. Antiserums were obtained from rabbits given repeated intravenous and subcutaneous injections of virus-containing fluid. In proper dilution these antiserums neutralized 100–1,000 CID_{50} of homotypic virus only. Isolates exhibiting hemadsorption were tested in aliquots containing 100–1,000 CID_{50} for neutralization by these four antiserums. Four isolates were typed for us elsewhere as indicated below.

Test for neutralizing antibody. Serums were heated at 56° C. for 30 minutes with the exception, where possible, of that aliquot tested against CA virus, because heat inactivation has been reported to markedly decrease titer of this antibody (*6*).

For screening, equal volumes of serum in 1:8 dilution and viral antigen containing 100–1,000 CID_{50} per 0.1 ml. were mixed and held at 4° C. for 30–60 minutes. Two-tenths milliliter of the mixture was added to each of two monkey kidney cultures, and after incubation at 37° C. for 4 days, the cultures were washed and tested for hemadsorption. Serums were thus screened simultaneously against the four viruses. Virus titrations accompanied each day's test.

Antibody titrations were similarly performed using serial twofold serum dilutions. Dilutions were considered positive for neutralizing antibody when hemadsorption was prevented in both cultures.

Results

Isolations. Data pertaining to the isolations are summarized in the table.

During July, August, and September 1959, specimens were collected from 322 patients.

Isolation of 13 hemadsorbing agents from 343 infants and children hospitalized in New Orleans

Specimen source and No.	Date collected	Culture system					Virus type	Clinical diagnosis	Source of negative specimens collected from same patient
		Cell culture				Egg			
		MK	FL	HeLa	HAM				
T77	May 1959	+	−	−	0	−	U	Nonbacterial meningoencephalitis.	F, CSF
F307	July 1959	+	0	0	0	−	HA1	Membranous tonsillitis.	T
T377	do	0	0	⊞	+	−	U	Mumps	F, CSF
T457	do	+	⊞	+	⊞	−	HA1	Sepsis, organism unknown.	F
F459	do	+	0	0	0	−	HA1	Lead encephalopathy.	CSF
T480	do	⊞	⊞	⊞	+	−	HA1	Congenital heart disease with left to right shunt ?Pneumonia.	F
T730	August 1959	+	0	0	0	−	U	Croup	F
T852	do	0	0	+	0	−	HA1	Dermatitis	F
T1066	Sept. 1959	+	0	0	0	−	U	Anemia unknown cause and "Leukemoid reaction"	F
T1191	March 1960	+	−	−	−	0	Flu A2	Croup	
T1194	do	+	−	−	−	⊞	Flu A2	Croup	
T1195	do	+	−	−	−	⊞	Flu A2	Croup	
T1196	do	+	−	−	−	0	HA1	Croup	

NOTE: T—throat swab; F—rectal swab; U—unidentified; CSF—cerebrospinal fluid; HA1—hemadsorption virus type 1; Flu A2—influenza type A2; −—not tested or not satisfactorily tested (see text under Virus isolation); 0—negative; +—positive; ⊞—typing not attempted.

Hemadsorbing agents were isolated from eight. There was no clustering of these positive patients with regard to age, sex, race, residence, or diagnosis. Nonhemadsorbing, cytopathogenic viruses were isolated from 27 percent of the patients (enterovirus 14 percent, adenovirus 4 percent, herpes simplex 2 percent, unidentified 7 percent), but these viruses were not found in patients yielding hemadsorbing agents which were isolated from rectal as well as throat specimens. Occasionally HeLa or HAM cells were more sensitive than monkey kidney cultures.

From December through March 1960 throat specimens were collected from 20 croup patients. Four yielded hemadsorbing and hemagglutinating agents which Dr. William Mogabgab in the department of medicine typed for us by hemagglutination inhibition. Although an etiological association between certain myxoviruses and croup has been observed by others (*5–7*), the lack of a control group for these 20 patients precludes similar interpretation in this instance.

Serology. The percentage of those individuals showing neutralizing antibodies to the four virus types was not markedly affected by race, sex, or residence. The effect of age is shown in the chart.

The percentage of persons positive to HA1 increased rapidly during the younger ages to approximately 90 percent at 10 years. For Sendai, on the other hand, the percentage of persons positive, although rising steadily with age, did not exceed 15 percent. Similar patterns between these extremes were found for CA and HA2.

Of the 286 persons with HA1 antibodies, 123 showed no antibodies to any of the other three agents. Seven of the 142 positive for CA, 6 of the 74 positive for HA2, and none of the 36 positive for Sendai showed a similar monotypic pattern. Seven persons showed antibody to Sendai and HA1. Titrations of these serums simultaneously against Sendai and HA1 revealed a higher titer for HA1 in every case. Similar tests made with 8 of 81 positive for HA1 and CA only and with 8 of 17 positive for HA1 and HA2 only revealed that in each instance the HA1 titers equaled or exceeded those for CA or HA2.

Heat inactivation of human serum has been reported to decrease appreciably CA virus antibody titer (*6*). No difference in titer was observed between heated and unheated aliquots of eight CA positive serums. These serums, however, had been frozen and thawed on a number of occasions. No similar testing for effect of heat was performed on aliquots to which fresh normal serum had been added.

Discussion

Heterotypic responses in humans following myxovirus infections have been observed by others, and these findings must be considered here because of their importance to the question of the specificity of the serologic data.

For example, Chanock and others (*2, 3*) have observed that in a portion of children from whom HA2 was isolated and a satisfactory rise in complement-fixing antibody demonstrated, there also occurred quantitatively similar increases of antibody to HA1 and Sendai but not to mumps and CA. In children from whom HA1 was isolated with fourfold or greater antibody rise, heterotypic increases were rarely observed. Infection of children with either HA1 or HA2 did not result in rise in complement-fixing antibody to the group antigens of influenza A, B, or C, nor was influenza infection productive of complement-fixing antibody to culture fluid antigen of HA1 or HA2.

Cook and others (*15*) have shown that in nine adults, four of whom had known infections with HA1 and five with HA2, antibody response was also frequently heterotypic. Pre- and post-infection serums were tested for complement fixation employing "viral" and "soluble" antigens and for infectivity neutralization of four parainfluenza strains, mumps, and Newcastle disease virus (NDV). There were no rises to mumps or NDV. Frequent heterotypic parainfluenza rises, quantitatively similar to the homotypic rise to the complement-fixing antigens, were observed. By neutralization test there were also heterotypic increases, but the homotypic response was quantitatively, consistently, and in most instances markedly, greater.

Increase in hemagglutination inhibition antibody to Sendai virus has been observed in adults, following mumps (*16*), and in patients with infectious mononucleosis (*17*).

Thus, the presence of antibody is no guarantee of prior homotypic infection. Evidence that at least some of the positive tests for HA1, HA2, and CA antibody were indicative of homotypic infection comes from the six isolations of HA1 reported here, and from Dick and others (*10*), who have recently isolated HA2 and CA from adults in the New Orleans area. In addition, in some individuals only one type of antibody was detected.

The probability that the relatively few positive tests for Sendai antibody represent heterotypic responses is indicated by the following considerations. To our knowledge Sendai virus has been isolated only in the Far East and in Moscow. As this agent may be primarily isolated in eggs by widely used, conventional influenza techniques, it is unlikely that it as yet exists far outside these areas. Hemagglutination inhibiting antibodies have been demonstrated in a large proportion of human serums collected from a wide area of the United States (*18*). Because this work preceded recognition of the newer myxoviruses closely related to Sendai, it is not known to what extent these antibodies were the result of heterotypic response. In the present study, all of the relatively few persons showing Sendai neutralizing antibody had antibody to at least one other parainfluenza virus. In those showing antibody to HA1 and Sendai only, the titer to HA1 was the higher in each instance.

It is of interest that while our isolations were chiefly HA1 for children, Dick and others (*10*) working with adults found HA2 and CA but not HA1. The agreement of these observations with the serologic findings suggests that the vast majority are infected with HA1 and become immune to it during their first 10 years, whereas most adults are susceptible to infection with HA2 and CA. Whether this pattern occurs generally is not known.

Summary

Thirteen hemadsorbing agents were isolated from 343 infants and children hospitalized in New Orleans, La., between May 1959, and April 1960. Six of these isolates were typed as hemadsorption virus type 1 (parainfluenza type 3), three as influenza type A2 and four were unidentified.

Serums from 380 other residents of southern Louisiana were tested for neutralizing antibodies to four of the parainfluenza viruses. The percentages of these individuals showing antibodies to HA1, croup associated, HA2, and Sendai viruses were 75, 37, 19, and 9, respectively.

The findings of this study as well as those of similar studies reported in the literature indicate the presence in southern Louisiana of HA1, CA, and HA2 viruses but not of Sendai.

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Migratory Labor

Domestic agricultural migrants and their families number nearly 1 million persons—a population as large as that of any one of 15 States—who live and work for varying periods of time each year in about 1,000 counties, largely concentrated in 31 States. The estimate is that there are from 350,000 to 500,000 children who belong to these families. . . .

Migrants may move across State and county lines several times during each crop season. They live in isolated places in temporary housing that is often substandard. They stop overnight by the roadside on long trips between work locations, with no facilities for decent human living. Their periods of work are frequently interrupted when weather and other conditions make work impossible. Income per worker annually averages less than $1,000. . . .

Access to education and medical and hospital care is often barred by their isolation, lack of transportation, failure to qualify for public assistance, and ignorance of where to go or how to find help. For some, difference in language creates additional barriers.

Migrant agricultural families—and particularly their children—constitute the most educationally deprived group in our Nation. Among adult members of the families, illiteracy is extremely high, and there is lacking even basic training in healthful living. This condition in itself would constitute a severe educational handicap for the children, but there is the additional fact that the opportunity to attend school is often denied these children. Such educational opportunities as may be available are often of an intermittent character. The vast majority of these children never attain the bare minimum of education needed to take part in our society. . . .

Efforts have been made by some communities to adapt their local health services to the facts of migrant families' living and working conditions. . . .

The usual approach is on an emergency basis. A child's death from insecticide poisoning attracted newspaper reporters to a migrant labor camp within an hour's drive of Chicago last summer. The child was almost forgotten as reporters discovered the depressed conditions of migrant families. Housing hardly fit for human beings served as their temporary "homes."

Within a short drive of any one of a number of cities, closely similar conditions could be found during each crop season. The families live at our back doorstep, unnoticed and forgotten. . . . The need for action in the educational and health areas is urgent.—*Excerpt from statement by* ABRAHAM RIBICOFF, *Secretary of Health, Education, and Welfare, before the Subcommittee on Migratory Labor of the Committee on Labor and Public Welfare, U.S. Senate, April 13, 1961.*

Salmonella infantis Isolated From Ham in Food Poisoning Incident

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AN OUTBREAK of gastroenteritis occurred among eight members of a family in Cincinnati, Ohio, in June 1960. Epidemiologic investigation by the Hamilton County Board of Health revealed that a 5½ pound portion of smoked ham was purchased from a supermarket about 12 noon, June 17. The ham was taken home and refrigerated at approximately 60° F. Between 1 p.m. and 6 p.m. of the same afternoon, the eight persons ate either raw or fried slices of ham. Peas, cream-style corn, bread, coffee, and milk were available, but the only food eaten in common was ham. Within 8 to 23 hours after ingestion, the members of the family suffered some symptoms of gastroenteritis characterized by vomiting, diarrhea, fever, and prostration. All eight members experienced acute diarrhea, but hospitalization was not required. A physician was called and the Hamilton County Board of Health was notified of the outbreak.

The uneaten portion of the ham was obtained by the board of health for bacteriological analysis. A sanitarian was sent to the supermarket to report on its general sanitation level and to gather any additional epidemiologic information related to the outbreak. He reported that the meat storage box in the supermarket was dirty. It was operating above 50° F. and was overloaded. A few of the hams were in contact with hot electric light bulbs, causing them to drip melted fat.

Although food-poisoning outbreaks are not investigated routinely by the milk and food research laboratory of the Public Health Service's Sanitary Engineering Center, the epidemiologic evidence in this instance presented an interesting research opportunity; therefore, the invitation to participate was accepted.

We have observed that the routine laboratory examination of foods incriminated in outbreaks of gastroenteritis is often inadequate. Generally, these examinations are perfunctory because the laboratory workers may be unfamiliar with the necessary procedures for performing a critical microbiological analysis or they may be unaware of the significance of the numbers as well as the types of organisms present. Therefore, the following report of our investigation is presented in detail.

Bacteriological Analysis

A portion of the raw ham was examined in the laboratory 2 days after the outbreak occurred. Thirty grams of the ham was placed in 270 ml. of sterile, phosphate buffered dilution water (*1*) and blended for 2 minutes at slow speed in a Waring Blendor cup. The resulting 1:10 dilution was examined microscopically by Gram's stain and the blend analyzed as follows.

Total aerobic count. Appropriate tenfold dilutions were prepared and plated in duplicate in Bacto-plate count agar, and the plates were incubated 48 hours at 35° C.

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Coliform count. Decimal dilutions were plated in duplicate in Bacto-violet red bile agar and incubated 24 hours at 35° C. Dark red colonies, at least 0.5 mm. in diameter, were counted and confirmed by inoculating into tubes of brilliant green lactose bile broth which were incubated 24 hours at 35° C.

Fecal streptococci. Decimal dilutions were plated in duplicate in Bacto–KF streptococcus agar (*2*) and incubated 48 hours at 35° C. In addition to the plate-count method, an MPN determination was performed by transferring 1.0-ml. portions from each selected dilution of sample into five tubes of azide dextrose broth and incubating 24 and 48 hours at 35° C. Confirmation was made by transferring a loopful of broth from each positive tube in the last three positive dilutions to a tube of ethyl violet azide broth and incubating at 35° C. for 24 and 48 hours and observing for turbidity (*3*).

Staphylococcal count. The surfaces of duplicate plates of Bacto-staphylococcus 110 agar were inoculated with 0.1-ml. aliquots of each decimal dilution. The aliquots were spread evenly over the surface with a sterile, bent, glass rod. The plates were incubated 48 hours at 35° C. The ratio of pigmented to nonpigmented colonies was determined for each of the countable plates, and representative colonies of each were picked and tested for coagulase production in the same ratio.

Salmonellae count. One-tenth-milliliter aliquots of each of the decimal dilutions were spread evenly over the surface of duplicate Bacto-brilliant green agar plates containing 0.06 mg. of sulfadiazine per milliliter to suppress the growth of *Proteus*, *Pseudomonadaceae*, and coliform organisms (*4* and personal communication from M. M. Galton, 1958). The plates were incubated 24 hours at 35° C., and the number of pink colonies was recorded. In addition to the plating procedure, 1.0 gm. of ham was placed in 9.0 ml. of Hajna's tetrathionate broth (*5*) and incubated for 24 hours at 35° C. as a pre-enrichment technique. Growth from the tetrathionate broth was streaked onto duplicate plates of the brilliant green agar described above and incubated 24 hours at 35° C. Typical *Salmonella* colonies were picked from both sets of brilliant green agar plates, and the isolates were identified according to the biochemical and serologic schema of Edwards and Ewing (*6*).

Clostridia. One milliliter of the original 1:10 blend was inoculated into duplicate tubes containing 15 ml. each of Bacto-fluid thioglycollate broth which was steamed 10 minutes just prior to inoculation to drive off dissolved oxygen. The broth was incubated for 24 hours at 35° C. A loopful of growth from the thioglycollate broth was streaked onto duplicate plates of 5 percent rabbit blood agar and McClung-Toabe egg yolk agar (*7*). Both sets of plates were incubated 24 hours at 35° C. in a Case Anaero Jar (*A*), under an atmosphere of 90 percent nitrogen and 10 percent carbon dioxide (*B*). Following incubation, the blood plates were observed for hemolytic colonies (both incomplete and complete hemolysis) and the egg plates for lecithinase-producing colonies.

Production and Assay of Enterotoxin

This laboratory has evolved over the years a fairly reliable assay for testing the enterotoxicity of staphylococcal culture filtrates based on the cat test. This assay requires the injection of 5.0 ml. of culture filtrate into the saphenous veins of four cats (4 to 5 pounds each). Cultures are considered positive for enterotoxin when they elicit vomiting in at least three of the four cats, between 20 minutes and 3 hours after injection. This procedure consistently yields positive results with filtrates of *Staphylococcus aureus*, 196E and S6, known as enterotoxigenic strains. A modification of Casman's (*8*) medium is used to produce toxic filtrates because the injection of unaltered medium sometimes results in the death of cats. The modified medium is composed of K_2HPO_4, 0.05 percent; KH_2PO_4, 0.05 percent; $MgSO_4 \cdot 7H_2O$, 0.01 percent; l-cystine, 0.0025 percent; sodium acetate, 0.35 percent; l-tryptophane, 0.0075 percent; casamino acids (Bacto), 1.0 percent, and the following concentrations per liter of Ca pantothenate, 500 micrograms; thiamin HCl, 40 micrograms; nicotinic acid, 1,200 micrograms. The medium is adjusted to pH 7.2 to 7.4 with 0.1 N NaOH and sterilized at 121° C. for 15 minutes.

Toxic filtrates produced from the modified

Types and numbers of bacteria isolated from raw ham incriminated in an outbreak of gastroenteritis

Type of determination	Medium	Number of organisms per gram of ham
Total aerobic plate count.	Plate count agar	268, 000, 000
Coliform bacteria	Violet red bile agar. Brilliant green lactose bile broth.	15, 000
Fecal streptococci	KF streptococcus medium.	31, 000, 000
Fecal streptococci MPN.	Azide dextrose broth. Ethyl violet azide broth.	31, 000, 000
Staphylococci [1]	Staphylococcus 110 agar.	200, 000, 000
Salmonellae [2]	Brilliant green agar. Tetrathionate broth.	23, 000
Clostridia	Blood agar plates. Egg yolk plates.	0

[1] An eight-to-one ratio of white to yellow colonies observed; neither type was coagulase-positive.
[2] Identified serologically as *Salmonella infantis*.

medium are obtained from shake cultures grown in an atmosphere in which 30 percent of the air is replaced with CO_2 as follows: 2 ml. of a 24-hour staphylococcal nutrient broth culture is added to 25 ml. of medium in a 125-ml. Erlenmeyer flask. This flask is partially evacuated, and 30 percent of the original volume of air is replaced with CO_2. The flask is then incubated for 24 hours at 35° C. on a reciprocating shaker operating at 120 strokes per minute. After incubation, 5.0 ml. of this culture is used to inoculate a second 125-ml. Erlenmeyer flask containing 25 ml. of medium, which is gassed as described above and incubated for 6 hours at 35° C. on the shaker. After 6 hours' incubation, 3.0 ml. of culture from the second flask is added to each 100 ml. of medium in a 500-ml. Erlenmeyer flask. The final flasks are similarly gassed and incubated at 35° C. on a reciprocating shaker (100 strokes per minute) for 4 days. It is possible to produce 1,200 ml. of toxic culture broth in a 6-liter Erlenmeyer flask.

Following the final incubation, the cultures are centrifuged at 3,000 rpm for 20 minutes to remove the cells. The supernate is passed through a Seitz filter, collected, and heated for 30 minutes in a boiling water bath. After cooling, the filtrates are injected into cats as previously described. The staphylococci recovered from the ham were tested for enterotoxin production by the above procedures.

Results

The results shown in the table summarize the bacteriological data obtained from the sample of ham. Though the total bacteria count was exceedingly high it was composed mostly of staphylococci and fecal streptococci. The isolated staphylococci, both pigmented and nonpigmented, were tested for coagulase production with negative results. Both types of colonies were cultured in modified Casman's medium and tested for enterotoxin production by the cat test with similarly negative results.

Only one streptococcal species, *Streptococcus faecalis*, and only one *Salmonella*, *Salmonella infantis*, were isolated from the ham.

These data indicated that the organisms present in significant quantities in the ham were the staphylococci, enterococci, and salmonellae. Little significance was attached to the staphylococci because none of 18 colonies tested (8 white and 1 yellow per countable plate) yielded positive coagulase reactions. In addition, the separate testing of mixtures of yellow colonies and mixtures of white colonies for enterotoxin yielded negative results. Because of the large number of enterococci present, and the well-known pathogenicity of the *Salmonella*, these organisms were viewed with suspicion. Stool specimens were requested for examination, to help clarify the situation, but they were not available until 10 days after the outbreak. Of the eight persons affected, specimens were obtained only from the mother and father and two sons of grade school age living at home. The stools were examined for salmonellae and enterococci, employing the procedure described. Only one streptococcal species, *S. faecalis*, was isolated from the stools of both parents and one son. *S. faecalis* var. *liquefaciens* was the only one of the streptococci isolated from the stools of the other son. The number of enterococci in the feces ranged from 7 million to 35 million per

gram. Salmonellae were not recovered from the stools of the two boys; however, *S. infantis* was isolated from the feces of both parents.

Discussion

Though available evidence indicates that *S. faecalis* and its related varieties are associated with food poisoning, their role as etiological agents of gastroenteritis is not universally accepted. However, when they have been incriminated they have usually represented the predominant flora, with other types of food-poisoning organisms present in small numbers or undetected. In view of the inconclusive results obtained from feeding experiments conducted by various investigators (*9–13*), their real role is unknown. Nevertheless, until additional information is provided which unequivocally demonstrates whether this group of organisms is pathogenic or not, the presence of large numbers of alpha-type streptococci in foods incriminated in gastroenteritis outbreaks cannot be ignored.

The occurrence of salmonellae in processed poultry has been established by Galton and others (*14*), and surveys conducted by members of the Communicable Disease Center, Public Health Service (*15*), have shown the association of *S. infantis* with processed poultry. However, the occurrence of salmonellae in other meats is low (*4*, *16*, *17*), and in cured meats practically nonexistent. In a recent survey conducted at the Sanitary Engineering Center, none of 314 cured or prepared meat products yielded salmonellae (*18*). Of the salmonellosis outbreaks reported in the United States from 1956 through 1959, none was shown to be transmitted through ham (*19*). Thus, the occurrence of salmonellae in cured meats, particularly ham, apparently is a rarity in this country. For this reason, the isolation of *S. infantis* from the ham in this outbreak is noteworthy.

Though the oral infective dose for humans is unknown for *S. infantis*, an estimate is obtained from the data of McCullough and Eisele (*20*). They found that the oral infective dose for several species of salmonellae ranged from a low of 125,000 for *S. bareilly* to a high of more than 1 billion for *S. pullorum*. The *S. infantis* concentration in the ham in this outbreak was estimated as 23,000 per gram. Assuming a 50- to 100-gram weight per slice of ham, the ingested number of salmonellae approach 1 to 2 million per slice. Two persons consumed three ham sandwiches each. Such concentrations conceivably approach oral infective dosages. The number of *S. infantis* recovered from the ham, the prolonged incubation period, and the isolation of this organism from the stools of some of the patients is evidence for establishing a *Salmonella* etiology in this instance. Because the ham was in the home for less than 1 hour before a portion of it was eaten and because of the significant number of *Salmonella* it contained, the ham was assumed to be the original source of infection to the family. However, no attempt was made to establish the existence of a carrier in the family or to establish the possible origin of contamination for the ham.

The presence of enterococci and salmonellae together in the ham presents the possibility of a mixed infection. Though the weight of evidence incriminates the *Salmonella*, the possibility of a mixed infection or an enterococcal etiology cannot be excluded.

This outbreak lends further support to our theory, derived from observation of previous reported outbreaks in which implicated foods contained large numbers of enterococci and relatively small numbers of other pathogenic bacteria, that associative growth between certain enterococci and other organisms may possibly contribute to the development of typical food-poisoning symptoms. For example, investigation of an outbreak aboard an interstate common carrier revealed large numbers of enterococci and some *Clostridium perfringens* in the implicated turkey dressing (*21*).

Evidence is not currently available to weigh the significance of associative action in enterococcal outbreaks. However, if such a condition is necessary, it may account for the failure of many pure cultures of enterococci to cause illness when fed to volunteers in past investigations.

Often, in the performance of a laboratory analysis of foods incriminated in food-poisoning outbreaks, only the staphylococci are sought and merely the presence or absence of coagulase-positive types are reported. We should

like to stress again the importance of the number of organisms present, as well as the type, in a suspected food. Coagulase-positive staphylococci are not uncommon in perishable foods, and the reporting of their presence with no reference to numbers per gram is insufficient evidence to establish the etiology of an outbreak. The incubation periods of staphylococcal, enterococcal, and clostridial types of food poisoning are so similar and overlapping that their use for determining the type of organism to be sought in the food may lead to erroneous conclusions.

The latest figures from the National Office of Vital Statistics of the Public Health Service reveal that approximately half of all the reported food-poisoning outbreaks are classified as "unknown etiology." This situation may be remedied by more intensive analysis of the foods involved. Examination of foods implicated in outbreaks of gastroenteritis should include detection and enumeration for enterococci and clostridia. However, the presence of these organisms in food is not uncommon, and, as with the staphylococci, an estimate of the number present is necessary before their role can be assessed. Instances in which large numbers of these organisms are found, or in which they constitute the predominant flora, may be considered significant. Though salmonellae normally are present in small numbers in some raw foods, their presence in cooked foods or foods which receive heat treatment sufficient to destroy them is particularly noteworthy. However, here again an attempt should be made to enumerate the salmonellae in order to determine the numbers which are associated with cases.

Summary

Investigation of an outbreak of gastroenteritis affecting eight members of a family revealed that the only food eaten in common was ham. Bacteriological examination of the ham disclosed that the organisms of significance present in large numbers were *Streptococcus faecalis* and *Salmonella infantis*.

Stool specimens of the persons affected contained large numbers of *S. faecalis*. Stools of two of the patients were positive for *S. infantis*.

The contamination of ham with *S. infantis* is noted because of its rarity, and the data available indicate the outbreak was due to either a mixed infection of enterococci and salmonellae or to *S. infantis* alone.

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British Editor Prescribes Vigorous Writing

American physicians should write in the same vigorous language they use in speaking, advises Dr. T. F. Fox, editor of *The Lancet*, in an interview reported in *Medical World News*, March 31, 1961. "What they say aloud is usually concise and effective . . . yet when the American takes pen in hand, he all too often seems constrained to use a sort of scientific literary language which conceals sense instead of displaying it," says Dr. Fox.

"In my opinion, the writer is not writing as himself—as a human being, as a person—but in the pretentious way he thinks fitting for an author. . . .

"I believe that real harm has been done to medical practice by teaching doctors to think in terms detached from people. It is this that leads to Mrs. Smith becoming, in the doctor's mind, the case of splenomegaly in bed 61—at which point the human relationship is broken.

"In *The Lancet* we prefer that the facts not be disguised—that patients be called patients, not subjects, or material, or a series. And if people have to die, I'm against efforts to escape reality with phrases such as 'proceeded to a fatal termination'. . . .

"We should base our writing on our speech. Language is primarily something spoken, and only the highly expert should venture far from the straightforward terms in which we instruct our wives, reprove our children, and tell the baker how many loaves to deliver."

Preliminary Tests With DDVP Vapor for Aircraft Disinsection

DARRELL R. MADDOCK, M.S., VINCENT A. SEDLAK, B.S., and H. F. SCHOOF, Ph.D.

EFFECTIVE disinsection of aircraft is essential to prevent the introduction of nonindigenous insects into the United States. Present disinsection procedures rely on the treatment of passenger and baggage compartments by means of aerosols. Despite the toxicity of such aerosols to insects, experimental treatments of the baggage compartments of planes have shown that the percentage kill of test houseflies is not adequate, even at levels 10 to 20 times the dosages normally used.

Other types of insecticidal applications have been studied as possible substitutes for the aerosol technique, but the only one of promise was that reported by Quarterman and Sullivan (*1*). They found that vapor from lindane-treated filters installed in the ventilating system of an aircraft gave excellent kill of free-flying houseflies at an exposure period of 30–60 minutes and at concentrations of 0.09 to 0.16 μg. of lindane per liter of air. Since that time, considerable work (*2*, *3*) has been done to explore the feasibility of using insecticidal vapor for aircraft disinsection. The toxicant used was DDVP. As one of the steps in this comprehensive study, a series of tests was conducted on the ground with commercial aircraft of the DC–6 and DC–7 types at the Miami International Airport in 1959.

The DDVP vapor was produced by experimental dispensers (see illustration), which consisted of a squirrel cage fan (10 cfm) attached to a polyethylene flask containing purified DDVP and a wick of coarsely woven fiberglass fabric (*4*). Air from the fan passed into the flask through a polyethylene tube inserted in the apex of the wick and then was discharged to the exterior through one or two side ports. The wick through which the air passed was saturated with DDVP.

Since initial tests indicated that the installation of such a vaporizer at each end of the passenger compartment did not provide adequate distribution of the DDVP vapor, the vaporizer was attached to the exterior of the plane so that the discharge of the vaporizer was directed into the intake of the ground ventilating system. During the course of each treatment, the ventilating system was in operation. According to information supplied by Pan American World Airways, Inc., the ground ventilating system provided approximately one exchange of air every 3 minutes.

Houseflies were exposed in tubular wire-screen cages (3.5 inches in diameter and 4 inches high) closed with paper covers. Twelve to sixteen cages, each holding approximately 200 flies of mixed sexes, were positioned from

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Dr. John Porter, Division of Foreign Quarantine, Public Health Service, Miami, Fla., obtained insectary facilities and was instrumental in making the cooperative arrangements with the Pan American World Airways, Inc. John C. O'Neal, facilitations superintendent, Pan American World Airways, Inc., made arrangements for the aircraft used in these tests and extended numerous other courtesies to the investigators.

the front to the rear of the passenger compartment as follows: in baggage racks, on the floor in relatively unprotected places, underneath and on seats, and in cloakrooms and lavatories. Generally three or more tests were run in the same plane before another plane was used. Following several of the tests, flies were placed in screen wall cages and exposed to various types of interior surfaces to ascertain the persistence of any DDVP residues thereon.

To determine concentrations of DDVP vapor, analysis was made of air samples collected 2 feet above floor level during the entire 30-minute test period (*5*). Thus, the air concentration data represent the average air concentration during the 30-minute fly exposure period.

Results

The data for six tests conducted in the passenger compartment of a DC–6B aircraft (3,600 cu. ft.) are given in table 1. Since the average kill of test 2 was less than 70 percent, the fan motor of the vaporizer for test 3 was insulated to increase the temperature of the air, thereby increasing the rate of DDVP vaporization. When only a slightly increased kill was obtained, two vaporizers with insulated motors were used in test 4. Despite the apparent absence of any increase in the average vapor concentration over that of test 3, the average mortality for test 4 was 96 percent.

In the second series of three tests (5, 6, and 7), in which two vaporizers also were employed, 100 percent kills were obtained at all sites except two, where the levels were 96 and 99 percent. Vapor concentrations were in a range of 0.11 to 0.28 μg. per liter of air. However, knockdown observations on the caged flies indicated a progressive increase in vapor concentration, the knockdown time (KDT_{50}) averaging 18.5, 18.0, and 14.9 minutes for tests 5, 6, and 7, respectively. Temperature rose from 74° to 81° during the sequence of the three tests.

Table 1. Average percent mortality of caged Musca domestica of mixed sexes exposed to DDVP vapor at 12 sites in the passenger compartment of a DC–6B aircraft, Miami, Fla.

Test No.	Temperature (°F.)	DDVP (microgram per liter)	Average 24-hour mortality (percent)
2	76	0.14	67
3	76	.28	75
4	77	.28	96
5	75	.28	100
6	74	.25	99
7	81	.11	100

Table 2. Average percent mortality of caged Musca domestica of mixed sexes exposed to DDVP vapor at 12 sites in the passenger compartment of a DC–7B aircraft, Miami, Fla.

Test No.	Temperature (°F.)	DDVP (microgram per liter)	Average 24-hour mortality (percent)	
			All sites	Exclusive of cage site in cloakroom
9	78	0.22	72	81
10	79	.17	75	85
11	79	.18	79	91
12	80	[1] .31	87	96
13	85	.35	97	99

[1] Based on single air sample.

Data for the tests in a DC–7B passenger compartment (4,200 cu. ft.) are given in table 2. A single vaporizer was used in tests 9, 10, and 11, and two units in tests 12 and 13. Vapor concentrations were approximately the same in tests 9–11 with average fly mortality ranging from 72 percent to 79 percent. In tests 12 and 13 vapor concentrations were similar, the average kill in test 12 being 87 percent and in test 13, 97 percent.

The kills obtained in tests 11 and 12 were 80 percent or higher at all sites except in the cloakroom. The latter gave the lowest mortality in all tests, but in test 13, it showed a kill of 86 percent. The poor kills in the cloakroom chiefly arose from the fact that, in contrast to the DC–6B, this area in the DC–7B was not serviced by an air duct. If the cloakroom site is omitted, the average mortality is increased 9 to 12 percent in tests 9–12 (table 2).

Thirty minutes after three consecutive tests (5, 6, and 7), in a DC–6B determinations were made on the persistence of DDVP in the air and on the compartment surfaces. Flies were exposed in screened tubular cages and in wall

cages fastened to vinyl plastic and stainless steel surfaces for this evaluation. The caged flies not in contact with a surface showed an average kill of 44 percent with a 40-minute exposure. With the same exposure time, wall cage tests gave an average kill of 60 percent. Most of the mortality obtained was due to the kill of the male flies. The concentration of DDVP was approximately 0.03 μg. per liter of air.

After each of tests 9–13, one or two wall cage tests were run on leather and on vinyl plastic surfaces using 30-minute exposures. Mortality ranged from 11 to 15 percent, 25 to 57 percent, 24 to 36 percent, 21 to 22 percent, and 5 to 38 percent, after tests 9, 10, 11, 12, and 13, respectively. Following 5 hours of ventilation of the aircraft after test 13, wall cage mortality on vinyl plastic and on leather was 0 to 5 percent.

Discussion

One of the significant points of these tests is the fact that DDVP vapor dispensed by an experimental vaporizer into the ventilating system of a commercial aircraft produced effective kills of the test specimens distributed at various sites and elevations in the passenger compartment. The dosages recorded indicate that against houseflies vapor concentrations of approximately 0.3 μg. per liter of air were highly effective. This concentration is somewhat higher than those reported from the tests in simulated aircraft (*3*), in which 0.15 μg. of DDVP per liter of air yielded a mortality of 95 percent or higher.

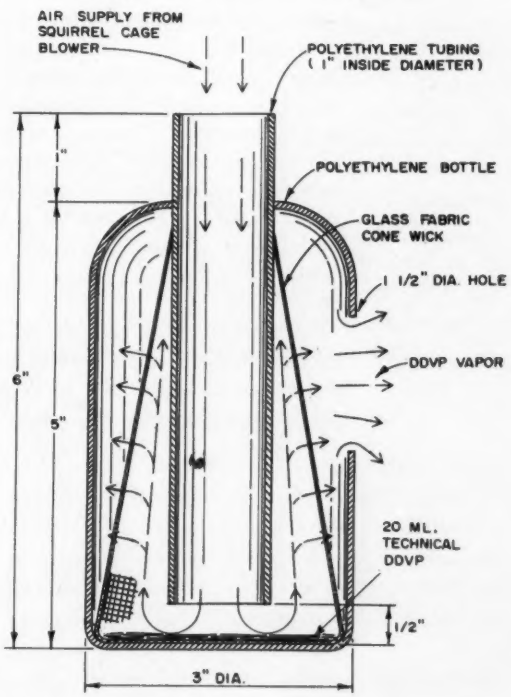
The relationship between KDT_{50} and 24-hour mortality was quite similar to that observed in earlier simulated field and laboratory tests (*3*). In these tests, a KDT_{50} of 18 minutes or less forecast female kills of more than 94 percent. During the present tests, a KDT_{50} of less than 18 minutes indicated 100 percent mortality of both sexes, a KDT_{50} of less than 23 minutes, 95 to 100 percent. At KDT_{50}'s between 26 and 30 minutes, the mortality was above 94 percent in only 2 of 15 observations.

Treatment of the aircraft with DDVP at the concentrations recorded was not perceptible to the workers after the initial minute. The four participants in this work remained in the passenger compartment during the entire period of all treatments and did not notice any adverse effects. The absence of any effects was expected in view of previous studies (*6*) in which six individuals exposed for 1 or 2 hours on each of 4 consecutive days to an average concentration of DDVP vapor of 2.1 μg. per liter of air showed no effect except for a questionable lowering of the plasma cholinesterase in two individuals. Under the same conditions an average concentration of 0.2 μg. of DDVP per liter of air was required for effective kill of houseflies exposed for 30 minutes.

Data from the persistence tests indicate that the vapor produces transient residues on the interior surfaces, which soon dissipate. The vinyl plastic surfaces tested retain vapor residues much more readily than do other surfaces, such as upholstery, carpet, and curtains (*4*).

The results of these tests indicate the feasibility of using an insecticidal vapor for the effective disinsection of aircraft. The principal advantage of such a method is that the toxicant can be dispersed throughout the passenger com-

Experimental DDVP vaporizer



partment area without depending upon crew or quarantine personnel for this operation. In addition, the preliminary data suggest that the vapor disinsection would be far less objectionable to the passengers and crews than the aerosol method currently used for that purpose.

Based on the present findings, future studies on the vapor method of disinsection should point toward the development of a dispensing unit that would be wholly mechanical in operation, that preferably would not employ the toxicant as a free liquid, and that would be suitable for permanent installation in the aircraft. Concurrent with or following such studies, detailed tests on the toxic hazard of such a unit would be required.

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Planning Long-Term Care Facilities

A joint committee to develop principles and recommendations for planning of facilities for long-term patient care has been formed by the American Hospital Association and the Public Health Service. The first meeting was held July 25–26, 1961, in Washington, D.C. The 17-member committee is headed by Ray E. Brown, superintendent of the University of Chicago Clinics and past president of the AHA.

According to State Hill-Burton hospital construction authorities, there is a national shortage of more than one-half million beds for long-term care. This number is expected to grow as the aged population increases. Moreover, many nursing homes are structurally below standard and do not provide all the necessary types of services and care.

Through the new committee, the American Hospital Association and the Public Health Service hope to establish guidelines that will help national, State, and local groups plan for adequate long-term care facilities coordinated with the community's health program.

Drinking Water Standards, 1961 Revision

The 1961 revision of the Public Health Service Drinking Water Standards includes for the first time limits for concentrations of radionuclides in water. Limits for several new chemicals, including some types of synthetic chemicals, also have been added. This revision, the first since 1946, is the work of a special advisory committee of physicians, scientists, engineers, and administrators, with assistance from a technical subcommittee of Public Health Service officers and a toxicological task force.

The Public Health Service Drinking Water Standards were first formulated in 1914 to protect the health of the traveling public. They have been revised at irregular intervals since that date, and their use has become widespread. In view of the accelerating pace of technological developments affecting water quality, the 1961 revision committee recommends that a mechanism be established for continual appraisal and appropriate revision of the standards.

Controls on Radioactivity

Recognizing that the effects on large population groups of chronic exposure to low concentrations of radioactive materials are not yet well defined, the committee set limits which it considers conservative, based on the best information now available. They may be adjusted upward or downward as new and better data become available.

The concentrations of radionuclides specified for drinking water, shown in the tabulation below, are intended to limit intake of these substances by this route so that total radiation exposure of population groups does not exceed the values given in the appropriate Radiation Protection Guides recommended by the Federal Radiation Council.

Radionuclide	*Concentration ($\mu\mu c./l.$)*
Radium 226	3
Strontium 90	10
Gross beta activity (strontium 90 and alpha emitters absent)[1]	1,000

[1] Negligibly small fraction of the above specific limits, where the limit for unidentified alpha emitters is taken as the limit listed for radium 226.

Concentrations of radionuclides which exceed, on the average, the specified values for 1 year constitute grounds for rejection of the water supply. However, where the total intake of radium 226 and strontium 90 from all sources has been determined, these values may be adjusted by appropriate authorities so that the total intake of radium 226 and strontium 90 will not exceed 7.3 $\mu\mu c.$ per day and 73 $\mu\mu c.$ per day, respectively.

When mixtures of radium 226, strontium 90, and other radionuclides are present, the specified values must be modified to assure that the combined intake is not likely to result in radiation exposure in excess of the values recommended by the Federal Radiation Council.

Limits for Chemical Substances

The new revision of the Drinking Water Standards includes two types of limits for chemical substances: limits which should not be exceeded when more suitable supplies are or can be made available at reasonable cost and limits which if exceeded are grounds for rejection of the supply.

The following concentrations should not be

The information presented here is taken from the report of the Advisory Committee on Revision of the Public Health Service 1946 Drinking Water Standards.

exceeded when in the judgment of appropriate authorities other more suitable supplies are available:

Substance	*Concentration (mg./l.)*
Alkyl benzene sulfonate (ABS)	0.5
Arsenic (As)	.01
Chloride (Cl)	250.0
Copper (Cu)	1.0
Carbon chloroform extract (CCE)	.2
Cyanide (CN)	.01
Iron (Fe)	.3
Manganese (Mn)	.05
Nitrate[1] (NO_3)	45.0
Phenols	.001
Sulfate (SO_4)	250.0
Total dissolved solids	500.0
Zinc (Zn)	5.0

[1] In areas where nitrate content of water is known to be in excess of the listed concentration, the public should be warned of the potential danger of using the water for infant feeding.

If concentrations exceed the values listed below, the water supply is subject to rejection:

Substance	*Concentration (mg/l.)*
Arsenic (As)	0.05
Barium (Ba)	1.0
Cadmium (Cd)	.01
Chromium (Cr^6)	.05
Cyanide (CN)	.2
Lead (Pb)	.05
Selenium (Se)	.01
Silver (Ag)	.05

Recommended control limits for fluoride in water are based on air temperatures. When fluoride is naturally present in drinking water, the concentration should not average more than the appropriate upper limits in the table below. Presence of fluoride in average concentrations greater than two times the optimum values constitutes grounds for rejection of the supply. For water supplies that are artificially fluoridated, the average fluoride concentration must be kept within the upper and lower control limits.

Annual average maximum daily air temperature[1]	*Fluoride concentration (mg./l.)*		
	Lower limit	*Optimum level*	*Upper limit*
50.0–53.7	0.9	1.2	1.7
53.8–58.3	.8	1.1	1.5
58.4–63.8	.8	1.0	1.3
63.9–70.6	.7	.9	1.2
70.7–79.2	.7	.8	1.0
79.3–90.5	.6	.7	.8

[1] Based on temperature data for a minimum of 5 years.

The advisory committee considered the inclusion of limits for the more common chlorinated hydrocarbon and organophosphate insecticides, but the information available was not sufficient to establish specific limits. Moreover, the concentrations of these chemicals wherever they were tested have been below values that would constitute a known health hazard. The committee believes, however, that pollution of water supplies with such contaminants might become significant and urges that the problem be kept under close surveillance. The committee also recommends that regulatory actions be taken to minimize concentrations of such chemicals in drinking water.

Damaged on Arrival

Please advise *Public Health Reports* when copies fail to arrive clean and whole. We shall be glad to replace damaged copies. Since a protective wrapper would add considerably to the expense of distribution, we plan to continue to mail the journal open unless the incidence of damage justifies a change. Epidemiologically speaking, preventive action does not seem warranted by the data available.

Use of Reference Samples in Evaluating Water Laboratories

ARNOLD E. GREENBERG, S.M.

UNDER REGULATIONS adopted in 1951 (*1*) water laboratories in California must be approved by the California State Department of Public Health if their findings are to be accepted by a health jurisdiction. Development of the regulations and proposed methods of operation under them have been described by Hartmann (*2*). As was observed, satisfactory operation of an approval program requires adequate methods for assessing work quality both prior to and after granting approval. Use of reference, or check, samples has proved the single best means of meeting this need. Since 1952, reference samples, either for chemical or bacteriological analysis, have been distributed to these laboratories, which now number 107. Results obtained from analysis of these samples have formed the basis for additional control measures.

The Analytical Reference Service of the Public Health Service has more recently developed a similar reference program for State laboratories (*3*). The national program, however, is voluntary, whereas in California participation is a condition for obtaining and maintaining an approved status. Also, the national program has as a major goal the evaluation of methods, while the California program is principally for control of work quality.

As an example of how the California program operates and to show generally how reference samples may be used, a detailed description is presented of one chemical reference sample, distributed in January 1960 to the 63 laboratories approved for chemical analysis. This report summarizes and evaluates the results obtained by the participants.

Mr. Greenberg is chief of the sanitation and radiation laboratory, division of laboratories, California State Department of Public Health, Berkeley. Roland L. Giusti, assistant chief of the laboratory, and Marjorie Lollich, division analyst, assisted in conducting the program and analyzing the data.

Preparation of Sample

Ideally a reference sample should contain known amounts of the constituents to be sought (*3*). Unfortunately, because of the large volume required, it was impractical to prepare a standard solution. Instead, the laboratories were sent replicate 1-gallon samples of water bottled in clean, dry containers at a water treatment plant handling surface water. An instruction sheet, which was also the report form, accompanied each sample. Analyses for calcium, magnesium, sodium, potassium, alkalinity, chloride, and sulfate were required, but not all laboratories made all analyses. The laboratories were asked to treat the reference sample as they would routine samples except each analysis was to be made in duplicate. Details of the methods used, the initials of the analyst, and the laboratory worksheet were also requested. In the sanitation and radiation laboratory of the State health department each of seven chemists individually analyzed the reference sample in an attempt to provide basic information on its composition and the variability of results.

Results

A summary of the results obtained is shown in table 1. In calculating the mean and standard deviation for the participating laboratories, a two-step procedure was used (*4*). First, the averages of all paired values were used to calculate the grand mean and standard deviation

for each constituent. Second, all values differing from the grand mean by more than ±2 standard deviations were excluded, and the mean and standard deviation were recalculated. This procedure is open to statistical question, but in practice it serves to eliminate an undue influence of gross and obvious errors such as dilution errors. The coefficient of variation expresses the standard deviation as a percentage of the mean.

Data on analytic methods used by the laboratories are summarized in table 2. Here, the mean and standard deviation were calculated conventionally; therefore, the data in tables 1 and 2 are not directly comparable. The data in table 2 are useful, however, in comparing different methods for the same constituent. For all constituents except alkalinity one method was definitely the predominant choice among the laboratories. For calcium and magnesium, it was EDTA titration; for sodium and potassium, flame spectrophotometry; for chloride, Mohr titration; and for sulfate, the gravimetric procedure. In determination of alkalinity the number of laboratories using the pH meter and the number using methyl orange indicator were about equal. These generalized observations closely parallel those obtained by the PHS Analytical Reference Service (*3*). With few exceptions the methods used were in accordance with Standard Methods (*5*).

Discussion

Inspection of the data in table 1 shows that results obtained in the State health department laboratory were less variable than those obtained by the participating laboratories. In the State health department laboratory there were only two major sources of variation: (*a*) differences between replicate samples and (*b*) differences between analysts in the same laboratory using the same methods. For the other laboratories the sources of variation were more numerous and possibly more significant. They were: (*a*) differences between replicate samples, (*b*) differences between laboratories, (*c*) differences between analysts, (*d*) differences between methods. Because of these differences, results of each laboratory were compared with those obtained by all the participating laboratories rather than with the results of the State health department laboratory. Therefore, the means and standard deviations for the approved laboratories shown in table 1, calculated by the two-step procedure, do not include results of the State health department laboratory.

Results of the duplicate analyses made by each laboratory were in most instances identical or very similar. Therefore, no statistical analysis was made of the paired values. Judging by the initials of the analysts given on the reports, the duplicate analyses were generally made by one chemist, although in a number of laboratories two or more chemists participated. Laboratory worksheets submitted by the laboratories proved quite useful. First, they permitted an examination of analytic details and recordkeeping procedures, and second, all results which were grossly deviant from others could be checked. In a number of re-

Table 1. Summary of results obtained on analysis of reference sample by the sanitation and radiation laboratory of the California State Department of Public Health and approved water laboratories in the State

Constituent	Sanitation and radiation laboratory			Approved laboratories		
	Mean (mg./l.)	Standard deviation (mg./l.)	Coefficient of variation (percent)	Mean (mg./l.)	Standard deviation (mg./l.)	Coefficient of variation (percent)
Calcium	46. 0	0. 675	1. 47	46. 5	1. 87	4. 02
Magnesium	21. 3	. 499	2. 35	21. 2	2. 54	12. 0
Sodium	75. 0	1. 52	2. 03	75. 9	4. 25	5. 60
Potassium	3. 8	. 180	4. 76	3. 5	. 67	19. 1
Alkalinity	84. 1	1. 80	2. 14	89. 5	3. 82	4. 26
Chloride	114. 1	1. 33	1. 16	114. 6	3. 24	2. 83
Sulfate	110. 5	2. 03	1. 84	109. 8	5. 44	4. 96

ports significant arithmetic errors were found and corrected.

For evaluating the performance of the participating laboratories the following arbitrary criteria were used: (*a*) results falling between the mean and ±1 standard deviation were acceptable; (*b*) results between ±1 and ±2 standard deviations from the mean were acceptable but questionable; and (*c*) results outside the limits of ±2 standard deviations were unacceptable. A summary of performance by these criteria is shown in table 3. Of the 63 participating laboratories, 1 laboratory produced unacceptable results for 6 determinations, 1 for 4 determinations, 1 for 3 determinations, 7 for 2 determinations, and 19 for 1 determination. Thus 29 laboratories, or 46 percent, produced unacceptable results for one or more constituents. These laboratories will receive continued close scrutiny.

On a percentage basis the mean of the results on calcium reported by the participating laboratories was essentially equal to the mean of the results obtained in our laboratory (46.5 v. 46.0 mg./l.). The frequency distribution of high and low values was about equal, although the number of unacceptable results, eight, was high. Surprisingly, the results obtained by EDTA

Table 2. Summary of methods used in analyzing a reference sample by approved water laboratories in California

Constituent and method [1]	Laboratories using method		Mean (mg./l.)	Standard deviation (mg./l.)	Coefficient of variation (percent)
	Number	Percent			
Calcium:					
EDTA	45	75	46. 2	2. 10	4. 54
$KMnO_4$	9	15	46. 4	3. 39	7. 30
Gravimetric (CaO)	4	7			
Flame*	2	3			
Magnesium:					
EDTA	40	67	21. 9	5. 22	23. 9
Gravimetric ($Mg_2P_2O_7$)	9	15	21. 8	1. 44	6. 61
Colorimetric (titan* or brilliant yellow)	6	10	20. 2	1. 35	6. 68
Flame*	2	3			
Unknown	3	5			
Sodium:					
Flame	40	74	74. 4	8. 38	11. 3
Gravimetric	8	15	77. 0	1. 73	2. 25
Calculated	4	7			
Spectrographic*	1	2			
Unknown	1	2			
Potassium:					
Flame	42	79	3. 6	0. 61	17. 1
Cobaltinitrite	8	15	2. 6	2. 58	98. 7
Spectrographic*	1	2			
Gravimetric*	1	2			
Unknown	1	2			
Alkalinity:					
Electrometric	29	45	89. 4	3. 07	3. 44
Methyl orange	22	34	87. 7	8. 98	10. 2
Mixed indicator	5	8	89. 5	3. 84	4. 29
Methyl purple*	4	5	85. 6	2. 10	2. 45
Unknown	5	8			
Chloride:					
Mohr	43	69	116. 3	5. 55	4. 77
Mercuric nitrate	15	24	108. 2	5. 40	4. 99
Electrometric*	3	5			
Unknown	1	2			
Sulfate:					
Gravimetric	44	75	110. 6	6. 39	5. 78
Titrimetric	7	12	110. 2	5. 38	4. 88
Turbidimetric	6	10	114. 5	16. 2	14. 2
Unknown	2	3			

[1] All methods except those marked with an asterisk are from Standard Methods (*5*).

titration with various indicators were less variable than those obtained by the combined gravimetric-$KMnO_4$ standard titration method, but the mean values were almost identical.

For magnesium the mean obtained by the participants was essentially the same as ours (21.2 v. 21.3 mg./l.). Grossly deviant high values appeared more frequently than comparable low values. The overall variability of results was unexpectedly high, but the number of variant laboratories was among the lowest (table 3). From table 2 it can be seen that this high variability is due principally to variations in results of the EDTA titration. Explanations for the difficulty are not obvious, but it may be related to choice of indicator.

Table 3. Number of approved water laboratories in California with questionable or unacceptable results on analysis of reference sample

Constituent	Questionable results [1]	Unacceptable results [2]
Calcium	16	8
Magnesium	8	5
Sodium	16	5
Potassium	15	8
Alkalinity	16	5
Chloride	18	7
Sulfate	16	8

[1] Between ± 1 and ± 2 standard deviations from the mean.
[2] Greater than ± 2 standard deviations from the mean.

The mean of the values obtained for sodium by the participants was almost identical with ours (75.9 v. 75.0 mg./l.). High and low values seemed to be equally distributed although all unacceptable values were low ones. Results obtained by the gravimetric procedure were less variable but higher than those of spectrophotometry.

The mean for potassium obtained by the participants was significantly lower than ours (3.5 v. 3.8 mg./l.). More unacceptable low results were produced than unacceptable high results. Most of the unacceptable results were obtained by means of a cobaltinitrite procedure. Unfamiliarity with the methods of determining potassium, a determination which is not often made, probably accounts for these results.

For alkalinity the mean obtained by the participants was significantly higher than ours (89.5 v. 84.1 mg./l.). This discrepancy may be attributed to the pH selected as the end point of the titration. Dong and associates (*6*) have shown the errors resulting from selection of an end point which does not correspond to the equivalence point of the bicarbonate titration. We used a pH of 4.8. If, in the absence of any data, it is assumed that the pH used by the participants was that of methyl orange, 4.3, and the correction suggested by Dong and his coworkers is applied, then the average alkalinity for the participants becomes 83.7 mg./l. It may be concluded that many of the apparent discrepancies in the results are due to end point selection rather than real errors. The average results obtained with methyl purple (table 2), which changes color at pH 4.8, tends to support this belief. From table 2 it may be further concluded that the use of methyl orange as the end point indicator is generally less satisfactory than the use of a pH meter irrespective of the pH selected for the end point.

The two means for chloride were essentially identical (114.6 v. 114.1 mg./l.). The frequency of high and low values appears normal. Both the Mohr and mercuric nitrate methods were equally variable, but the mercuric nitrate titration gave lower results, on the average, than the Mohr titration (table 2).

For sulfate the two means were again essentially identical (109.8 v. 110.5 mg./l.). The gravimetric procedure yielded higher and considerably less variable results than the turbidimetric methods.

To check independently the correctness of any analysis, the simple anion-cation balances method of Greenberg and Navone (*7*) can be used. Although this was not done for each laboratory it was done for the averages of all the laboratories. The average sum of the cations (7.45 meq./l.) compares favorably with the anion sum (7.31 meq./l.), indicating overall acceptability of results.

This reference sample showed that performance by a small number of laboratories was, on the whole, unacceptable. Further, it demonstrated that performance of a larger number of laboratories was better, but occasionally unacceptable. With this information, the State health department laboratory was able to insti-

tute a followup program to improve those laboratories needing it.

Initially, we wrote a letter to each laboratory pointing out its deficiencies, if any, and urging immediate corrective action. Then we visited these laboratories to discuss their deficiencies, review their methods, and generally survey their operations. Repeat reference samples will be submitted to the laboratories to measure again the quality of performance.

This followup procedure has been used during the past year with all laboratories first applying for approval. Several of the laboratories initially denied approval were later approved as a result of significant improvements in their work.

Summary

To illustrate use of reference samples in California in assessing quality of work done by approved water laboratories, the story of one chemical reference sample distributed to 63 laboratories is presented. Calcium, magnesium, sodium, potassium, alkalinity, chloride, and sulfate determinations were required. Statistical analysis of the data permitted an evaluation of the quality of performance as well as yielding comparative information on analytic procedures.

Of a total of 63 participating laboratories 29 returned unacceptable results for one or more of the seven constituents. These findings were used as a basis for a program of closer supervision of the laboratories, with, it is hoped, a significant improvement in the quality of water laboratory work in California.

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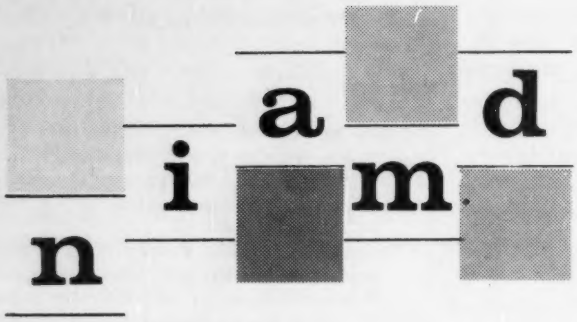
Research Grants in Radiological Health

A greatly expanded program of research grants to individuals, universities, laboratories, and other institutions, in radiological health, has been announced by the Division of Radiological Health, Public Health Service. These grants are offered to support studies in the assessment and control of manmade and natural radiation exposures to individuals. Research proposals should contribute to the determination of the extent and character of the radiation problem as well as to the mechanisms by which radiation produces damage.

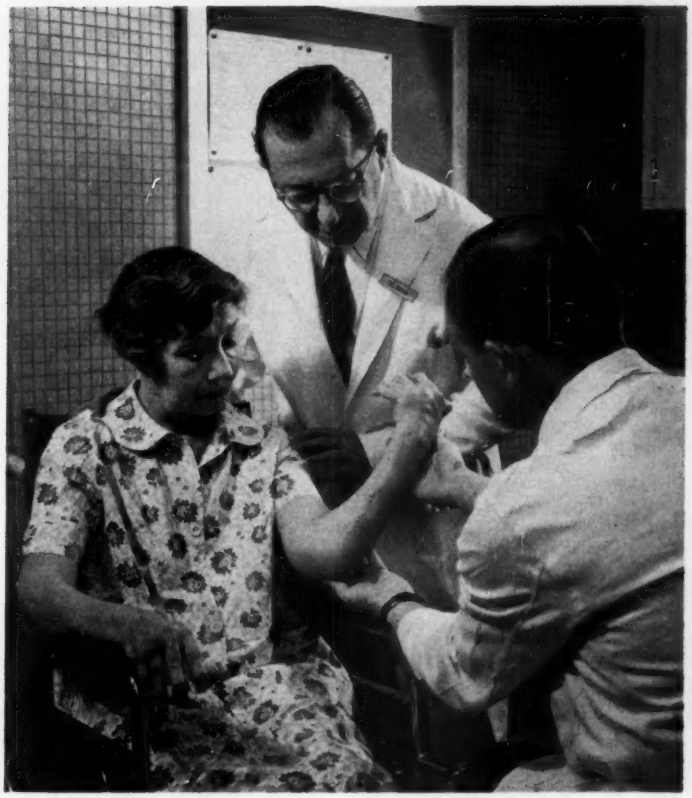
For information and application forms contact: Dr. Paul F. Hahn, Chief, Office of Extramural Grants, Division of Radiological Health, Public Health Service, Washington 25, D.C.



ten years

The National Institute of Arthritis and Metabolic Diseases of the Public Health Service recently celebrated its 10th anniversary with a public report to the Nation on research progress during the past decade. The institute was established in 1950 by the Omnibus Medical Research Act and resulted from a surge of interest in the arthritic disorders, spurred in large part by the discovery of cortisone. Although it was originally created for the study of arthritis and the then known metabolic disorders, the institute, located in Bethesda, Md., conducts and supports research in additional areas, including hematology, gastroenterology, cystic fibrosis, and in such basic disciplines as pharmacology, biochemistry, nutrition, and physical biology. The scientific accomplishments presented on the following pages indicate the wide scope of institute activities. They represent research conducted in the institute's own laboratories and by its grantee scientists throughout the country.

ADVANCE AGAINST ARTHRITIS



Dr. Joseph J. Bunim with arthritis patient

PREDNISONE, the first synthetic corticosteroid, was introduced into medicine by Dr. Joseph J. Bunim, clinical director of NIAMD, and his associates in 1954. This antiarthritic drug possesses important clinical advantages over the naturally occurring steroids, cortisone and hydrocortisone, because of a reduced tendency to cause retention of fluid when administered in conventional therapeutic doses. Prednisone and newer synthetic steroids, still under constant development, are largely replacing cortisone and hydrocortisone in the treatment of arthritis and allied disorders.

The cause of the connective tissue diseases remains unknown. But new work, stemming from the hypothesis of the Australian virologist Sir Macfarlane Burnet and research in the past decade, offers some possible clues. Burnet's theory concerns how disease results from an auto-immune process by which an individual develops antibodies against his own cells or tissues. Cells reproducing and mutating throughout life set up a constantly changing pattern of antibody-antigen formation which results in a never-ending problem of self-identification.

Two recent findings in the rheumatic diseases are significant although they do not prove the Burnet theory. The so-called rheumatoid factor, present in 85 percent of patients with rheumatoid arthritis, is a very large gamma globulin, possibly an antibody synthesized in plasma cells. It has been discovered that in systemic lupus erythematosus a whole series of antibodies is produced against many common nuclear constituents, particularly desoxyribonucleic acid, the genetic material. Researchers are testing to see if the facts of arthritis and lupus erythematosus support or clarify the Burnet hypothesis.

SYNTHETIC ACTH

THE SYNTHESIS OF ACTH may provide clues as to how this hormone teams up with cortisone to relieve arthritis. ACTH is produced by the pituitary gland, and its production stimulates the outer shell of the adrenal gland to release cortisone and other hormones into the system. Cortisone and cortisonelike drugs are used in the temporary remedial treatment of rheumatoid arthritis, rheumatic fever, and other diseases. But their specific action on these diseases is not yet known.

Until the synthesis was accomplished, only ACTH produced by animals or human beings was available for investigation and therapy.

Constructed in 1960 by biochemists at the University of Pittsburgh, the hormone has the biological activity of natural ACTH and represents the largest proteinlike molecule ever produced synthetically. Using many original devices, the NIAMD grantees constructed it by putting together 23 natural amino acids, the building blocks of proteins.

Researchers believe the new techniques can be used to modify the structure of ACTH to achieve medically important results. The synthesis may also pave the way for synthesizing even more complex proteinlike molecules and clarify the workings of the pituitary gland.

REMEDY FOR GALACTOSEMIA

THE BIOCHEMICAL cause of galactosemia, a rare but often fatal metabolic disorder in which children cannot utilize any form of milk in their diet, was discovered by Dr. Herman Kalckar and his associates at the institute in 1956. They found that galactosemic infants lacked a single enzyme in the blood needed to convert galactose to glucose, the sugar form used by the body for energy. This inherited enzyme deficiency results in the accumulation of an apparently toxic byproduct of galactose metabolism and accounts for the characteristic pattern of mental retardation, blindness, enlarged liver and spleen, and early death.

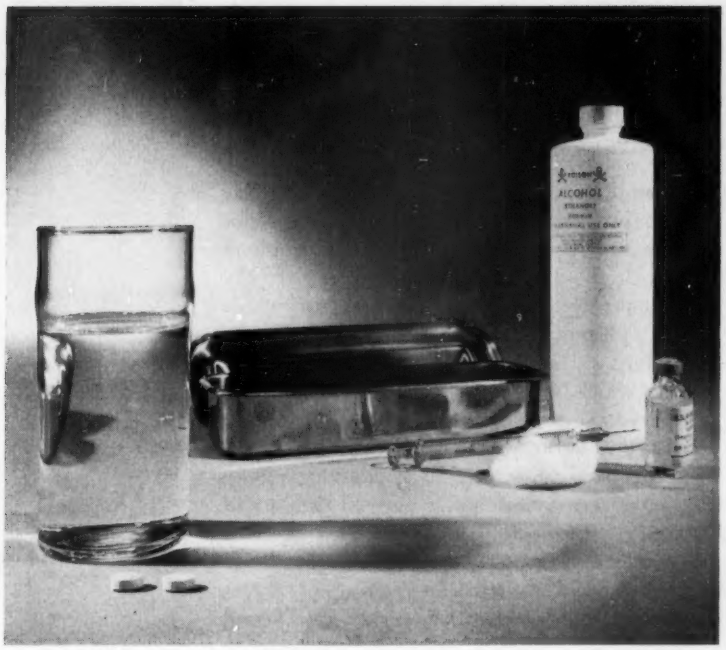
The biochemical discovery led to the development of a diagnostic test which has made it possible to diagnose the disease immediately after birth. This is essential, since the affected children will grow and develop normally on a milk-free diet. Continuing studies by other institute scientists have shown that injections of the female hormone, progesterone, enables galactosemic children to convert at least some galactose into glucose, and menthol has been found to have the same effect. These findings open the possibility that there may be ways to overcome this inherited defect and possibly others like it.

POWERFUL NEW PAINKILLER

DR. EVERETTE L. MAY, a chemist, and Dr. Nathan B. Eddy, a pharmacologist with NIAMD, have developed a potent new analgesic, phenazocine, which, is 5 to 10 times more powerful than morphine. The synthetic painkiller was derived from coal tar and has been clinically tested in thousands of patients. It relieves pain where optimal doses of morphine will not, and because of fewer and milder side effects it can be used for longer periods of time against chronic pain. Although it is a narcotic, phenazocine appears to be less addictive than the older drug; physical dependence develops more slowly and is less intense.

Phenazocine is one result of an intensive drug screening program at NIAMD which has evaluated nearly 8,000 compounds for their analgesic properties. Although not a final step, the new drugs represents significant progress toward the complete separation of the pain-relieving properties and the addiction potential of an analgesic drug.

Discovery of the synthetic drug also frees the United States from dependence on the foreign medicinal opium markets. Its developers have assigned all patent rights to the U.S. Government which has made them available to all countries.



PILLS ☐ REPLACE ☐ NEEDLES

☐

ORAL ANTIDIABETIC drugs introduced in the last 10 years have replaced daily insulin injections in 500,000 patients, more than one-third of the Nation's diabetics. However, these drugs are not effective in a great number of diabetics, and they are not the oral insulin that has long been sought. Although these drugs are widely used, the way they lower the high levels of blood sugar is not fully understood.

The first of the new hypoglycemic drugs, tolbutamide, became available in 1957 after intensive trials by institute grantees and other physicians. Since then two others have been introduced, chlorpropamide and phenformin. The development of these drugs by the pharmaceutical industry has had a far greater impact than that of merely providing a more convenient form of treatment for selected patients. The extensive laboratory and clinical research which preceded the debut of tolbutamide sharply focused attention on fundamental problems in metabolism, endocrinology, and biochemistry, and stimulated a new wave of research on this ancient disease.

For example, the first large-scale study of the natural history of diabetes, scheduled to continue for a minimum of 10 years, began in 1960. Approximately 700 patients, 100 at each of seven research centers, will participate. The study is now in the pilot stage. The University Group Diabetes Study will investigate the incidence and severity of late complications such as retinopathy, atherosclerosis, neuropathy, and kidney disorders.

Within its own laboratories the institute is continuing laboratory and clinical investigations of diabetes. In one study substances antagonistic to insulin have been found in the plasma of patients with diabetes mellitus who have never received insulin therapy. This and similar studies of insulin's mode of action shed light on an important possible cause of diabetes other than pancreatic inability to produce insulin.

SALT AND SODA FOR BURN SHOCK

A KITCHEN REMEDY for the emergency treatment of shock due to burns—drinking a solution of 1 teaspoon of table salt and ½ teaspoon of baking soda mixed in a quart of tapwater—was developed by Dr. Sanford M. Rosenthal, Dr. Kehl Markley, Dr. Herbert Tabor, and Dr. R. C. Millican of the institute. The simple therapy would be of particular value in a major disaster or in isolated areas since neither skilled personnel nor bottles of blood are required. It is not designed to replace the traditional treatment of injections of whole blood, plasma, or the so-called plasma expanders.

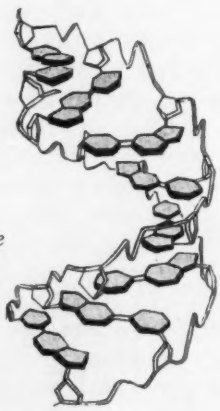
Burn shock, a semiconscious state marked by falling blood pressure and a lessening of the activities of vital body organs, accounts for a high proportion of the early deaths among victims of burns covering 10 percent or more of the body. From 1951 through 1959 the salt and soda solution therapy was evaluated clinically in burn shock victims in Peru. There were no deaths among adults. In infants, however, a combination of saline solution therapy with plasma was found to be more effective than saline solution alone or water and plasma alone.

Young Peruvian burn victim drinks salt and soda solution

CHEMISTRY OF HEREDITY

ONE OF THE ACHIEVEMENTS of basic research studies during the past 10 years was the biological synthesis of the genetic substances, DNA and RNA (desoxyribonucleic acid and ribonucleic acid). Dr. Arthur Kornberg, former chief of the institute's Laboratory of Biochemistry and Nutrition and now a grantee at Stanford University, succeeded in synthesizing DNA with the aid of a new enzyme which he discovered. Independently, Dr. Severo Ochoa, a grantee at New York University School of Medicine, discovered another enzyme which can synthesize RNA, and for their work the two scientists shared the 1959 Nobel Prize in Medicine.

It is now generally believed that DNA carries the "code" that directs the synthesis of all proteins and the development of the cell, determining whether the cell becomes a brain cell or a liver cell. Like a tape recording, DNA carries specific instructions for the life processes of the cell. It is the master template of nature from which exact copies can be made so that the information it contains can be used elsewhere in time and space. The making of these copies is the function of RNA.



DNA molecule

SYMPOSIUM ON WORLD MEDICINE

At the Symposium on World Medicine, held March 17–18, 1961, at New Haven, Conn., to celebrate the 150th anniversary of Yale University School of Medicine, the speakers outlined some of the major challenges facing the world's epidemiologists, immunologists, and virologists. Public Health Reports is printing, on the following pages, papers based on the addresses of six symposium participants. Proceedings of the conference will not be published.

Epidemiology and World Medicine

M. G. CANDAU, M.D.

I SHALL NOT attempt any precise definition of epidemiology either in its old or in its modern sense. I shall consider epidemiology as the study of the distribution of disease in large or small populations. It may, at one extreme, measure the broad prevalence of disease, nationally or internationally; at the other, it may examine small numbers of cases that present common features, such as blood dyscrasias caused by ionizing radiation. Between these extremes of mass statistics and small group studies lies a wide range of field and laboratory studies of many kinds, which, by epidemiologic methods and epidemiologic thinking, contribute to our knowledge of the etiology and mechanism of disease.

Epidemiology has achieved many important advances in recent years; it has broadened its scope and has extended its fundamental ideas. Its boundaries are now wider than its original territory of communicable disease, and its concern with noncommunicable disease, considered as a phenomenon of population, is progressively expanding. Epidemiology was formerly conceived of as primarily a concern with a specific infective agent; it now takes into account man's whole environment and his own reactions to that environment. In this way proper weight can be given to multiple causation, to the multiple interactions of innate characteristics and factors in the environment. This we might call the ecological approach, and it appears that it will be the most fruitful strategy for the future.

World medicine, the other half of the subject I am considering, is also a term with many possible meanings. It has been said that peace is indivisible, so also is medicine, and, as all physicians must feel, indivisible in a more immediate and practical meaning. All medicine is in a sense world medicine, for there is scarcely any advance in medical knowledge that does not affect the practice of medicine throughout the world. I am principally interested in the part played in world medicine by the World Health Organization.

The Organization is primarily an intergovernmental public health body and, in that capacity, carries on the traditional epidemiologic functions that it inherited from its predecessors. The foundation of any scientific work is a proper knowledge of the facts; the first step in the discharge of world epidemiologic functions is the collection of health statistics. WHO now receives regular statistical information on a substantially larger scale than that supplied to the League of Nations. For example, in 1938 causes of deaths were reported by 35 countries and territories; in 1959, by 108. The number of countries sending in reports on infectious diseases has also greatly increased; moreover, we now receive regular information

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about vaccinations and immunizations of various kinds from 160 countries and territories.

These reports are published monthly in the *Epidemiological and Vital Statistics Report* and, with further contributions from the United Nations and national statistical offices, in the *Annual Epidemiological and Vital Statistics*.

In order that the information received from the various countries may be as comparable as possible, WHO offers advice to countries as to the optimum methods of collecting and publishing their national statistics and encourages the use by all countries of uniform methods for these purposes.

International epidemiology had its origin in efforts to control the spread of the quarantinable diseases. Those pestilences now present less of a danger to world communications and world health, but improved control of an infectious disease does not necessarily reduce the responsibilities of the World Health Organization in regard to communicable diseases. When a disease is as widespread, for example, as measles still is, international or even national reporting is of relatively small immediate practical consequence. When the incidence of a given disease is reduced to a small compass, such as that of smallpox in many areas of the world, it becomes more than ever necessary to obtain and disseminate information about its occurrence so that international preventive measures can be taken quickly. A parallel is the great care that is necessary in tracing and dealing with the last few cases of a disease that is being eradicated from a country or region.

The control of influenza illustrates some special features. WHO obtains early information on any new outbreak of influenza and the number of cases; it also undertakes the important task of ascertaining what strains of virus are prevalent in each outbreak and of disseminating this information widely, so that an effective prophylactic may be prepared before the wave arrives. The work of Dr. A. M.-M. Payne at headquarters and of the influenza centers in many parts of the world showed clearly in 1957–58 the value of this system. In the near future we shall have to increase the work we are doing in the collection and dissemination of information on the prevalence of strains of other pathogenic viruses, such as poliomyelitis and the other enteroviruses.

Besides running this intelligence service, the Organization often aids the practical work of prophylaxis by assisting and coordinating vaccination campaigns and by encouraging the acceptance of uniform international standards of potency and safety for vaccines used in those campaigns.

A special interest in malnutrition is inevitable and immediate in a world health organization, and since the Organization was founded, we have done much work on this problem, usually in collaboration with other international organizations. In particular I mention our joint epidemiologic work with the Food and Agriculture Organization on kwashiorkor in Africa, Latin America, and India, which has led to the encouragement of research into ways of locally producing sufficient supplies of good quality vegetable protein.

More recently, WHO has turned its attention to the chronic diseases and particularly to cancer and cardiovascular diseases. Here its principal task, for the present at least, is to promote the standardization of nomenclature and techniques and to stimulate the study of differences in the incidences of cancer and cardiovascular diseases in different countries and ethnic groups, in the hope that such studies may provide a key to the better understanding of their etiology.

The World Health Organization has set up reference centers for mammary tumors, soft tissue tumors, and lung tumors, and plans are being worked out for a comparative study of the geographic pathology of several cancerous disorders. An example of this work is the study in Finland and Norway of the differences in the prevalence of lung cancer in urban and in rural areas.

Differences among certain countries in the prevalence of atherosclerosis were the origin of WHO's interest in cardiovascular diseases. This has already given rise to an international study, in several countries of the Americas and Europe, the object of which is to arrive at agreed uniform methods of grading pathological lesions. The Organization desires also to promote studies on the prevalence of ischemic

heart disease and arterial hypertension in different environments, with particular attention to comparisons between technically developed areas and areas, such as may be found in Africa, that are now undergoing rapid changes. Chronic cor pulmonale and the cardiomyopathies are other heart diseases for which WHO might usefully coordinate research. The multiple causes of cardiovascular diseases provide one of the best examples of the multiple interactions for which it will be necessary to work out the methods and techniques of identification. Similar international research is required in the study of psychosocial problems in areas that are disrupted by rapid urbanization and industrial development and in the study of mental disorders in general.

The Eleventh World Health Assembly in 1958 voted to intensify the Organization's program of medical research, and various groups of eminent scientists have given us valuable help in organizing that program. One of its main objectives will be to promote conditions in which knowledge and experience acquired by scientists in different parts of the world may be more readily compared and correlated by standardizing nomenclature, definitions, and techniques, and by using standardized reagents. In particular, we are examining what can be done to provide standard serums and reagents for use in virus research. In a rather different direction, we are assisting applied research by arrangements under which the manufacturers of promising new insecticides may have their products assayed and tested in laboratories designated by WHO. With the help of the National Institutes of Health, Public Health Service, some progress has been made with this scheme, which should materially reduce the interval between the discovery of a new insecticide and its use in the field.

Basic to the work of the World Health Organization in international public health, epidemiology, and medical research is its special role in relation to the "International Classification of Diseases." WHO has responsibility for arranging the successive revisions of this publication and for insuring that it remains continuously up to date and ready to serve the needs of its many users in almost every branch of health activity. I cannot emphasize too strongly that without an internationally established classification of diseases the interchange of health information between countries would be greatly impeded and international cooperation in epidemiologic research would be much less effective.

The Organization does not neglect the more traditional methods of insuring that medical progress may be extended to all parts of the world. It encourages the exchange of scientific information in publications, at meetings of scientists engaged in similar or related work, and by any other suitable means. It may be found that one of the most successful methods of aiding research is to bring men with special skills or experience to the places where those qualifications may be usefully applied to the local problems. In 1956, for example, a Tuberculosis Chemotherapy Center was set up in Madras, as a joint enterprise by the Madras State Government, the Indian Council for Medical Research, the British Medical Research Council, and the World Health Organization. Fourteen scientific papers have been published as a result of this enterprise, and nine more have been approved for release. It has been shown that, in communities where the living conditions are similar to those of Madras, domiciliary chemotherapy holds great possibilities for the successful treatment of tuberculosis. Fortunately the collaboration of those organizations is likely to continue for some years.

A special and important side of WHO's assistance to research is to help in the training of research workers. Its fellowship schemes have already given the Organization a good understanding of what developing countries need in the way of assistance to training, and of the resources available in developed countries from which those needs can be met. Training for research work is a special task and it still calls for careful study, but it is quite possible that this kind of assistance to training may prove to be the World Health Organization's most effective and material contribution to the advancement of medicine.

My purpose has been to show that in epidemiology and world medicine the World Health Organization has a definite part to play. I have sketched briefly the main lines of that part: col-

lecting and disseminating information (a process that often brings to light problems that require study), getting together research workers from different countries to work on common problems, providing services that will assist research, attacking research problems that are basically of international rather than national significance, and, possibly the most important of all, helping to train workers for research.

I believe that the Organization is in a good position to carry out those tasks. Its very structure allows it to obtain information from any part of the world in which there are medical problems that require investigation. Its staff represents a great diversity of cultures, inspired by a real international esprit de corps. But the main strength of the World Health Organization lies in the good will and collaboration of medical workers throughout the world. On this it has learned it can depend more than its most enthusiastic champions would have thought possible when the Organization came into being some 13 years ago. I am sure that WHO, in collaboration with medical workers in all countries, will continue to be worthy of this support.

Tine Test for Tuberculosis

The tine test for tuberculosis, which uses a new device for injecting tuberculin, appears to be superior to the patch test, according to Dr. Michael L. Furcolow, chief of the Kansas City Field Station of the Public Health Service Communicable Disease Center. He believes, however, that further work on the test will be necessary before it will be a satisfactory substitute for the Mantoux interdermal test.

Dr. Furcolow and his colleagues were one of four groups reporting studies of the new test at the annual meeting of the National Tuberculosis Association in Cincinnati, Ohio, May 21–25, 1961.

The new device is a stainless steel disk with four triangular stainless steel tines, all fitted into an inch-long, cylindrical plastic plug. The tines are coated with a concentrated filtrate of heat-killed tubercle bacillus and then dried. To make the test, the unit is pressed firmly against the skin allowing the tines to perforate it. After use the unit is discarded.

Since it eliminates the need for freshly sterilized needles and syringes, the new technique is faster and easier to administer than the Mantoux test. It is also possibly less frightening to children than use of the needle.

In a study of the accuracy of the new test, Dr. Furcolow and his colleagues found that 97 percent of 4,048 school children who were negative to the Mantoux test were also negative to the tine test using single-strength tuberculin. Only 77 percent of those positive to the Mantoux test were positive to the single-strength tine test, but agreement was increased to 92.3 percent when the standard double-strength tuberculin was used.

A clinical study of 800 sanatorium patients by Dr. D. C. Capobres and co-workers at Mount Vernon, Mo., found that the tine test yielded less than 5 percent false negatives and false positives compared with 22 percent false negatives on the patch test. Two other clinical studies, one by Dr. Sol R. Rosenthal of Chicago, who designed the steel disk, and the other by Dr. Edith M. Lincoln of New York City, indicate a correlation of 86 to 97 percent between the tine test and the Mantoux test.

SYMPOSIUM ON WORLD MEDICINE

The Profitable Enterprise

THOMAS PARRAN, M.D.

THE GENERAL THEME of this symposium can be expressed by a quotation from the 1951 WHO monograph entitled "The Cost of Sickness and the Price of Health." It was written by the late C.-E. A. Winslow, who contributed much to "the profitable enterprise" of public health in the United States and around the world.

A single sentence from this historic document states the theme: "A public health program adapted to the individual needs of each area offers the most economical means of breaking the chains of disease and poverty and initiating an upward cycle of social evolution."

The health scientists speak an international language, perhaps more clearly understood by what we call the underdeveloped nations than by us in the United States. When we all understand the objectives of world health, this understanding will contribute to unity among nations. For as Raymond Fosdick (*1*) once pointed out, uncontrolled disease anywhere in the world threatens the whole world. When a nation achieves a more healthful status, it takes nothing away from any other nation; on the contrary, it adds to productivity, gains a higher standard of living, and makes better education possible.

The theme of this conference deals with one scientific discipline, epidemiology, as it advances what the program planners call world medicine; I prefer the term "world health." The general objective is health, attained not only through the discipline of medicine but also through many other disciplines such as engineering, nutrition, biometrics, and a variety of the biological, physical, and social sciences—between which the lines of demarcation are growing dimmer—which constitute the domain of public health.

Because of the spectacular discoveries which have been made in the medical sciences recently, it is reasonable to anticipate that continued laboratory and clinical research will develop new preventive and clinical tools. Of equal urgency are searching epidemiologic studies to identify the environmental causes of unconquered disease in populations, and to direct the improved application of clinical knowledge, the broadly based organization of health measures, and the all-important impartial evaluation of results.

The vast advance of medical and biological science would have been impossible without specialization. But there is a reverse trend: the teamwork which brings skills from many narrow specialties to bear upon the disease process in a single patient or in a whole population. Frequently, however, at least some of the causes and cures of disease lie beyond the patient, and one must consider a complex of factors with impact upon the individual. This is particularly true of the chronic diseases in which a multiplicity of causes with biological, psychological, social, and other environmental components are operative over long periods. Such situations, and many others, cry out for topflight epidemiologists. Unfortunately for world health and local health, they are in short supply (*2*).

More and better practitioners of epidemiology are acutely needed. Consequently, it is gratifying to see at Yale that emphasis upon training and research in epidemiology is an integral part of medical education at all levels.

Dr. Parran, former Surgeon General of the Public Health Service, is dean emeritus of the Graduate School of Public Health, University of Pittsburgh.

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Many otherwise well-educated clinicians and surgeons still think of epidemiology as limited to turn-of-the-century epidemics of infectious disease. Yet the epidemiologic studies of scurvy, pellagra, and goiter go back many years (*2*). Those dealing with dental caries and amyotrophic lateral sclerosis, to mention two among hundreds, have the same fascination for a physician as a fast-moving detective story for the average layman. Moreover, we are now beginning to get substantial leads from epidemiologic studies in some aspects of mental illness (*3, 4*).

To enhance their literacy in these and other areas of preventive medicine, the 85 other medical schools in the United States could put to good use several dozen Dr. John Pauls.

It is also gratifying to see in the training of international students an emphasis upon flexibility so that they are prepared to deal with the limitations of the job at home.

While the excellence of a school or department of public health is not measured by the size of its budget, such a school is important to a great university medical center and merits unstinting support. It can and should enrich the curriculum of a school of medicine. It can expose both students and faculty not only to the vital discipline of epidemiology but also to a familiarity with biometrics, administration, and social components of the modern approach to disease control and eradication.

The faculty members of such a school are in constant demand to consult and advise in many parts of the world for varying periods. Hence, the school must be staffed in depth.

The success or mediocrity of public health graduates has prompt repercussions. Approximately 25 percent of the total number of students enrolled in the public health schools of the United States come from other countries. Of great significance is the excellence of their training here and their competence on the job at home, as well as the impressions they take home of the school, the university, and our Nation.

In world health, these are difficult times. On one hand is the possibility which man has sought for hundreds of years, relief from disease, disablement, and premature death. Even at the present level of knowledge, it is possible to eradicate malaria, yaws, smallpox, and manifestations of malnutrition. In due course, we can be free of tuberculosis, syphilis, leprosy, cholera, plague, and other ancient enemies which have decimated whole populations and sapped the vitality of those who survived. To do this will require a great effort, a united effort, and a well-financed effort.

On the other hand, the status of new nations and the play of power politics may inhibit progress already underway. I shall cite only one example, sleeping sickness. There is grave danger that excellent control measures instituted by Great Britain and France on a regional basis may be obstructed by the emergence of the many new African States in a single region.

Epidemiologic studies have shown, as pointed out by Morris (*5*), that "eradication of the disease can be achieved by vector control alone, if the control is complete; or by partial vector control plus chemotherapy, provided the attacks are well planned and simultaneous."

Yet increases in the amount and ease of transportation, new concentrations of people, the clearing of forests, and the extension of farming can force the tsetse fly into dangerously intimate contact with man in new nations without public health personnel or facilities. Meanwhile, the generations of a trypanosome are measured in hours, not years, and disease is no respecter of frontiers.

I agree with Morris that the solution of a problem like this "must lie in the action of a body, such as WHO, with the vision and status to put forward a realistic program of eradication on international lines" (*5*).

The "Health for Peace" Act, signed by President Eisenhower in July 1960, has many potentialities for international research. Supplementing less specific earlier legislation, it authorizes grants to scientists and institutions of other countries for research on health problems, whether or not we have similar ones in the United States.

Yet much more than research is needed, however broadly based that may be. Health and medical care programs must compete with other demands upon national and international budgets, not only for money but also for persons of intelligence and devotion. In recent years the number of applications to our medical schools

has decreased. Even more serious is the fact that able students are being diverted into more lucrative areas of postgraduate study which require shorter and less costly preparation.

The practitioner in world medicine needs special training after his internship, just as the fellow of the College of Surgeons or of the College of Physicians must have special training. For example, the epidemiologist, who is, perhaps, the keystone in the arch of international health, is a scarce commodity at all levels from students to professors. More interested medical leaders and more adequate training facilities are needed, but the major concern is to attract additional competent physicians, since the present facilities in our schools of public health, although limited, can train many more able students than apply.

The curriculums in most medical schools do not focus on the population aspects of health and disease; in addition the majority of medical students who show a capacity for research are promptly recruited by their professors for laboratory and clinical studies. The professors of epidemiology simply haven't been diligent proselytizers.

Although adequate manpower will not solve all the difficulties, if world health is to be a viable reality it needs an international civil service with adequate compensation, opportunities for professional advancement, and a program of refresher and retraining courses to keep up with new knowledge and changing situations. I can see no other feasible means of providing and retaining the necessary corps of devoted career workers to serve in many lands, often at a sacrifice of personal comfort. In such an international elite, the epidemiologist will have a central role.

Although it is a far cry from the highly trained and mobile group suggested, I cannot but hope that the recently announced Peace Corps may be a first steppingstone to recognition of the need for such workers. I know from my own experience that a consultant who goes to another country from a medical center here may provide a useful service; but he cannot fill the place of a man who is willing and able to spend his professional life at the task.

World medicine, the achievement of world health, is a full-time job for the best minds of our modern world.

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Bronfman Prizes

Establishment of a new series of awards for effective work in applying new scientific knowledge to community health, the Bronfman Prizes for Public Health Achievement, has been announced by the American Public Health Association.

From one to three prizes, made available by a grant from the Samuel Bronfman Foundation, Inc., will be awarded annually, depending on the availability of suitable candidates. Each prize will consist of a $5,000 cash award and a commemorative symbol.

In honoring application rather than discovery of new scientific knowledge, the foundation and the association hope to increase understanding and appreciation of public health practice.

The first awards will be announced and presented during the association's 89th annual meeting in Detroit, November 13–17, 1961.

SYMPOSIUM ON WORLD MEDICINE

Epidemiology in Latin America

ABRAHAM HORWITZ, M.D.

ACCORDING to Paul (*1*) it took about 4,000 years for epidemiology to emerge as a separate discipline which, by about 1920, was ready to stand on its own feet among the medical arts and sciences. Yet the concepts and principles that underlie modern epidemiology are essentially those laid down by the distinguished founders of the science.

The analytic reasoning of Snow, Panum, Goldberger, and Frost, to mention but a few of the outstanding workers in this field, continues to be applied today in order to gain a better understanding of man in health and in sickness, and, I think, must be even more extensively applied if we are to acquire a fuller knowledge of man as a social being.

As early as 1878, Hirsch (*2*) was describing historical and geographic pathology as "a science which . . . will give, firstly, a picture of the occurrence, the distribution, and types of diseases of mankind, in distinct epochs of time and at various points of the earth's surface; and secondly, will render an account of the relations of these diseases to the external conditions surrounding the individual and determining his manner of life."

This description might well be accepted as a definition of modern epidemiology, for, as Frost (*3*) pointed out, it implies that epidemiology is essentially an inductive science concerned not merely with the distribution of disease but equally, or more, with fitting it into a consistent philosophy.

Epidemiology, like all sciences of which speculation is a component, may be defined in a variety of ways. Such a multiplicity of definitions mirrors the richness of the material with which epidemiology deals, embracing as it does all events relating to human life, regardless of their origin. No matter how we choose to define it, the science of epidemiology as understood today encompasses the totality of man's relationships with his mediate and immediate environment, both in sickness and in health. In this sense, it is synonymous with medical ecology.

Epidemiology thus involves and facilitates an interpretation of life. And since the principles on which it is based have remained constant, what is changing are the circumstances under which diseases occur or do not occur, spread or do not spread; that is to say, the changes in environment and in adaptation to it that are characteristic of all living things.

Today there are many opportunities for epidemiologic studies in the New World, especially in Latin America. We Latin Americans like to refer to the Americas, so far as the distribution of diseases is concerned, as a continent in transition, a continent where the major quarantinable diseases are waning. No cases of cholera have as yet been reported in this century. In 1960, only 250 cases of plague were notified and most of those were sylvatic in origin; there were 650 reported cases of louseborne typhus, about 50 cases of jungle yellow fever, and less than 5,000 cases of smallpox. The incidence of other communicable diseases and diarrheal diseases is higher than we would wish, but already in most Latin American countries chronic diseases are emerging as an important

Dr. Horwitz is director of the Pan American Sanitary Bureau, Regional Office of the World Health Organization for the Americas. *The Boletin of the Pan American Sanitary Bureau is also publishing Dr. Horwitz's paper in its September 1961 issue.*

cause of death. Cancer, cardiovascular diseases, and accidents are now among the 10 major causes of death in these countries. There is an increase in life expectancy, growing industrialization, and rapid urbanization. But as a background to these rapid social changes, influencing health matters and being influenced by them, there stand the world's fastest rate of population growth, widespread illiteracy, a per capita income ranging from $100 to $500 a year, dependence on single commodity exports, inadequate investment, and the inevitable concomitants to these, poverty and misery.

There are many health problems in the Americas whose solutions are to be sought in the epidemiologic approach. In view of the geographic variations in diseases, there is not a single area in which epidemiology does not play an important role. I should like to mention, as illustrations, a few problems on which the Pan American Sanitary Bureau, Regional Office of the World Health Organization, is conducting basic epidemiologic studies.

To advance the epidemiologic study of diseases in the region, comparable mortality data are urgently needed. The appraisal of the quality of death certification, termed by Morris (*4*) "operational research," is now a matter of general concern. In the Americas we are going deeper into this problem, recognizing that the quality of death certification leaves much to be desired and hampers the comparability of mortality statistics. We plan to develop comparable data for selected cities by obtaining the complete clinical history and pathological findings for each death; medical certificates of death will be consistently completed and coded in accordance with international procedures. As a first step, investigators in 10 or more medical schools will develop centers in which teams of medical statisticians, epidemiologists, and pathologists will seek the essential data for epidemiologic studies. Once a full understanding of mortality has been obtained through age-adjusted death rates for specific diseases, research workers will begin to explore the factors responsible for such differences as are discovered. This coordinated research will enable selected medical schools to become centers for practical research and sound epidemiologic training. From such training centers, established preferably in departments of preventive medicine, a new generation of epidemiologists could come forth and could have a tremendous impact on medical science. A grant from the National Institutes of Health, Public Health Service, has been awarded for a planning conference to design these epidemiologic studies in the region of the Americas.

In cardiovascular diseases, regional research is underway to elucidate the natural history of atherosclerotic lesions found in population groups with widely different environmental and genetic backgrounds. Pathological laboratories in 11 countries, including the United States and several in Central and South America, are transmitting to a central laboratory specimens of aortas and coronary arteries obtained from necropsies. There they will be examined with a view to determining variations in atherosclerotic lesions according to age, sex, race, geography, nutritional state, and disease. This truly inter-American project is being carried out by the Institute of Nutrition of Central America and Panama and the faculty of medicine of Louisiana State University under the auspices of the National Institutes of Health. To date more than 2,500 aortas and coronary arteries have been examined.

As malaria recedes in the Americas under the impact of vast eradication programs, new epidemiologic difficulties are beginning to emerge, for disappearing malaria calls for new and intensive investigations. The fact that it is now possible to identify areas of stable malaria is evidence of progress, but that there are such areas despite well-conducted operations makes further epidemiologic research essential.

The persistence of malaria transmission in certain areas also demands further research on asymptomatic carriers, behavioristic changes in the anopheline's resting habits, outdoor transmission, and daytime transmission by certain vectors. The resistance of anophelines to insecticides and of plasmodia to drugs, as well as genetic variations in toxic susceptibility, are among the problems that confront us. Studies are also needed to evaluate medicated salt programs and to determine more accurately the therapeutic levels of antimalaria drugs for different species of plasmodia. The role of migratory laborers, of nomads, and of inacces-

sible populations in the persistence of malaria transmission is still to be determined.

Studies at the Institute of Nutrition of Central America and Panama show that a synergistic relation exists between malnutrition and infections such as diarrheal diseases, whooping cough, and measles, the total effect of which is a major cause of deaths in children under 5 years of age in many Latin American countries. Information about this relationship is fragmentary and circumstantial, and appropriate epidemiologic studies are needed to determine its scope as well as its implications for prevention. This problem is being investigated by INCAP in three communities in Guatemala. In the first, efforts are being made to reduce the burden of infectious disease by preventive measures, treatment, and improved sanitation. In the second, nutrition is being emphasized by the distribution of milk and other foods rich in protein and education in nutrition. The third community is being maintained as a control. It is expected that the results of this investigation will constitute a major contribution to our present knowledge in this field.

I should like to emphasize the acute need for epidemiologic research on medical care, especially in those Latin American countries where medical care activities are mainly financed from social security funds. Health needs and services must likewise be evaluated if long-range programs are to be planned. Virus diseases, mental illness, alcoholism, radiation hazards, and air pollution also offer enormous possibilities for research to determine their contribution to morbidity and mortality in the various countries. Such comparative epidemiologic studies would contribute to sound knowledge of the causation of diseases.

I wholeheartedly agree, so far as Latin America is concerned, with Morris (*4*) when he states that "epidemiology is today the Cinderella of the medical sciences" and that "the proposition must be advanced that public health needs more epidemiology; so does medicine in general, and, it may be said, society at large."

As to medical education, I do not feel that it would be unfair to say that epidemiologic thinking is given insufficient attention in the training of physicians and health officials. The dominant element in the teaching of medicine still appears to be the diagnosis and treatment of disease. Not enough attention is being given to medicine as a social science or to the study of man as a biological entity and a social being. As a result, analysis of the implications of health and disease for societies is only incidental to medical studies and is not impressed upon the mind of the student. He does not conceive of medicine as a harmonious balance between the prevention of disease, the treatment of the sick, and the promotion of health. The fulfillment of his responsibilities in modern society is more a matter of his intuition than the result of his understanding of disease in relation to the community.

In public health, epidemiology often becomes synonymous with communicable disease control. Practice and the application of knowledge overshadow analysis and speculation. Epidemiology is emphasized as a purely descriptive science. It is seldom being used to analyze common problems, irrespective of their origin, as they affect families, groups, and communities. Still less frequently is epidemiology considered an indispensable method for studying the workings of health services. The need to introduce more and better epidemiologic thinking into medical teaching and to prepare sound epidemiologists with a broad vision of the potentialities of the science is more than ever apparent. To this end, the international health organizations have a definite role to play, a role of major importance in restoring epidemiology to its true significance as a way of thinking and as an interpretation of life.

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SYMPOSIUM ON WORLD MEDICINE

Neglected Avenue to Knowledge

JAMES A. SHANNON, M.D.

EPIDEMIOLOGIC research has been applied in a most rewarding fashion to many health problems. In transmissible disease, such research has expanded understanding of causation and the mechanics of disease distribution, and together with allied sciences, has pointed to means for controlling epidemic spread in population groups and preventing disease in the individual. In human nutrition, from the strikingly effective studies of pellagra in the early decades of this century through a host of specific nutritional deficiencies to recent observations on kwashiorkor, epidemiologic research laid a firm foundation for the understanding of these complex diseases. An extension of such research in collaboration with allied sciences provided information on the specific nutritional deficiencies that led to rational therapy and prevention.

One might wonder, then, why this area of medical research, particularly in relation to world health, needs special highlighting by this symposium when the contributions have been characteristically major as well as worldwide in their genesis and application. I believe this might best be answered in light of certain problems that have increasingly concerned us all during the past decade.

This century has seen the development of means for the virtual eradication of transmissible and nutritional diseases as causes of premature death in both young and old and as serious barriers to socioeconomic advancement. Yet these diseases continue to be widespread and persistent. They can be expected to yield only to further heroic strides in the social and economic fields. Even here, however, the epidemiologic sciences can help in determining how present knowledge might be applied with the least disruption of existing or developing social patterns and at the least overall cost for a given result.

As infection and malnutrition are attacked with mounting effectiveness, chronic diseases have emerged as old problems with new dimensions. I have in mind the cardiovascular diseases, cancer, the disabling neurological complexes, mental illness, and others. Since the 1940's these disorders have increasingly occupied our medical investigators.

These studies have been highly productive in the identification of specific diseases and of correlations with related disorders. They have also contributed to our knowledge of the natural history of diseases, the biological basis of their manifestations, and the amelioration of disease or symptoms by medical agents.

On the other hand, studies to elucidate the ultimate causes have been less rewarding. A number of individual diseases have been adequately defined and broad general leads relating to causation have been uncovered and actively pursued. But mystery still surrounds the genesis of cancer in general, of hypertension and atherosclerosis, of the devastating demyelinating diseases of the central nervous system, of major psychiatric entities such as schizophrenia, and of such prosaic and common conditions as rheumatoid arthritis and gastrointestinal disorders.

Extensive and intensive research is being conducted on many fronts in the modern clinic and its intellectually adjacent laboratories. And yet, if one looks beyond these modern factories of new knowledge, he cannot but feel a lack of

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confidence that major breakthroughs and clarifying generalities will derive from a simple evolution of work already begun. It seems likely that we will require in addition a totally different kind of information.

During the past 5 years we have gone a long way in one direction, toward deeper penetration into the study of individual man. Notable in this phase has been the broad employment of physical sciences and their servant, mathematics, in the investigation of life processes. We must now move in an equally positive fashion to consider disease in the aggregate, particularly those factors that are contributed by man himself and his environment.

Such studies cannot be conducted solely in a conventional setting, but require comparative observations of disease development in population groups, that is, an epidemiologic approach. The population groups selected for study must be characterized by significant differences in their genetic composition, their physical environment, or their culture. In effect, we must bring the tools of the epidemiologist to bear upon the problems of chronic illness with an intensity not heretofore applied. Productive epidemiologic studies have been undertaken here and in other countries in order to define general factors associated with disease development. In evaluating such programs with a view to their possible extension, we must consider the obvious opportunities that are peculiar to the international scene.

It is considerations such as these, rather than the urgency to foster international good will, that should be the driving force in developing an adequate study program. Its importance should be judged by (*a*) the impact of the disease problems undertaken and (*b*) the prospects of success.

Lest this last point be misunderstood, let me add that I fully recognize the value of medical research as a platform for improving international understanding and good will. But the extent to which medical research will contribute to these ends, or detract from them, depends more upon the terms and conditions under which the studies are undertaken than on the substance of the studies themselves.

I will not try to enumerate the special opportunities open to epidemiology. I would simply state for the record that the opportunities have been generally appreciated by many scientists, in many fields, and for many years. Still, the logistics of support, which in the hands of the Rockefeller Foundation made such outstanding contributions over the first half of the century, have not been generally available.

For this reason I should like to list some conditions for what most of those who have given serious consideration to such programs would deem essential to success.

1. The programs must be staffed by our best investigators in the field and at home, and laboratories at field and home bases must be adequate and complementary.

2. They must be truly collaborative programs employing the scientific communities of the participating countries. It will frequently be necessary to provide broad training opportunity to scientists of the host country.

3. The programs must have long-term continuity, as contrasted with the characteristic "hit and run" tactics so frequently employed in today's international projects with narrowly defined targets. This will be possible only if we provide institutional careers in science wherein the international capabilities of individuals can be fully developed.

4. The programs must evolve with a deep understanding of the cultures of the peoples studied, so as to interpret properly the contribution of social as well as biological factors in the evolution of disease.

5. They must be more than parasitic; they should clearly recognize not only our needs and goals but those of the host country as well.

Parenthetically, it might be mentioned that these points were largely inherent in the research programs conducted by colonial powers as a necessary condition of the development of colonial areas. In our collaboration with independent countries and in the absence of a long-term medical service responsibility, we must still develop a cadre of knowledgeable scientists through some purposeful system oriented toward research. It will not happen in a wholly spontaneous fashion.

The five points listed were considered in the recent development of an international program of the Public Health Service. This provides

for the establishment of a limited number of international centers, broadly conceived and university based.

The centers will conduct research, initially of an epidemiologic nature but later developing as need and opportunity dictate. They will facilitate the welding of medical, biological, and behavioral sciences and have a broad capability for understanding and studying complex disease situations. Incidentally but importantly, the centers will develop and nourish a corps of well-trained and internationally oriented medical investigators for service to our country outside the areas of their specific and personal undertakings.

These centers represent a radical departure from the traditional mechanisms of support of international medical research through the use of Federal funds. They are made possible under the International Health Research Act of 1960, Public Law 86–610. An appropriation of some $5 million was made available to the National Institutes of Health, in part to develop this Program of International Centers for Medical Research and Training.

The law states the intent of Congress that the Public Health Service shall support health research and research training overseas and the objectives to be sought in overseas health research and training programs.

In substance, the program provides for the development of a range of highly stable international centers for medical research and training, with full opportunity for the development of productive careers. The centers will enable U.S. physicians and scientists to acquire broad field experience through projects conceived in ample breadth and duration. They will also encourage physicians and other health personnel of collaborating foreign institutions to participate in the development of health research and training resources in their national environment.

The two components of a center, the U.S. base and its overseas institutions, will have these characteristics: a U.S. university providing a stable professional framework in which medical research projects, planning, and training can be conducted, and associated research and training establishments overseas where these activities can be pursued under environmental, ethnic, and medical conditions that do not prevail in the United States.

The program is just getting underway. Funds are limited and our experience insufficient to warrant conclusions. But I believe the International Centers for Medical Research and Training will be particularly useful for developing international scientific manpower, for strengthening international operations already in progress, and for cementing relations among participating institutions and agencies. I am confident that they can fulfill in some measure the express hope of Congress for "a program through the U.S. universities for the early development of research and research training centers with adequate field opportunities for international studies."

School Teachers Health Manual

The "Brookline School Health Manual," a guide for the school teacher in her part in the management of accidents and communicable diseases in schools, has been issued jointly by the health department and the school system of Brookline, Mass.

A section on accidental injuries tells when injuries require only simple measures, when professional help should be called, and what the teacher can do. Sections on communicable diseases include information on signs and symptoms, cycles of infection, and prevention and control measures. The information is arranged in charts and is tab-indexed.

SYMPOSIUM ON WORLD MEDICINE

Arthropod-Borne Viral Encephalitis

WILLIAM McD. HAMMON, M.D., Dr.P.H.

THE VIRUSES causing the arthropod-borne encephalitides and other related disease syndromes form a group that might be considered the epidemiologist's dream. Epidemiologic studies of this group require the teamwork and knowledge of the epidemiologist, agriculturalist, sanitary engineer, ornithologist, mammologist, veterinarian, virologist, immunologist, and clinician.

In keeping with the theme of this symposium I will emphasize the worldwide aspects of the encephalitides. The scope will be broad rather than specific. I will discuss in general the range of clinical syndromes, the spectrum of vectors, the spectrum of epidemiologic patterns, determinants of geographic distribution patterns, currently recognized world distribution, the number of different viruses, and, briefly, prevention and control.

The term "arthropod-borne viral encephalitis" was introduced by Dr. William C. Reeves and myself many years ago to replace what we considered less suitable terms such as epidemic encephalitis, summer encephalitis, and arthropod-borne encephalitis. Recently I suggested a further change since many related viruses in the group produce diseases other than encephalitis and possibly all are zoonoses, with man the occasional and accidental host in the primary biological cycle of the virus.

This new term is the arthropod-borne viral zoonoses. To shorten this, several abbreviations have been suggested, the most common being "arbor" for arthropod-borne, but I prefer "arbo" since "arbor" is a Latin word and suggests that this is a disease of trees and is caused by a plant virus.

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Range of Clinical Syndromes

The range of human clinical syndromes caused by the arbo viruses is indicated in the following list. A few named viruses are given as examples in each of three categories. Nearly all the viruses in the encephalitides group and all those in the other two groups produce encephalitis in the laboratory mouse. The second category of clinical syndromes includes fevers with and without rash and sometimes with arthralgia, and the third category is a group of hemorrhagic fevers.

1. Encephalitides (essentially all produce encephalitis in mice): eastern encephalitis (EE), western encephalitis (WE), Venezuelan encephalitis (VE), St. Louis encephalitis (SLE), Japanese B encephalitis (JBE), and Murray Valley encephalitis (MVE).
2. Fevers with and without rash: dengues, Colorado tick, West Nile, phlebotomus, Mayaro, Chikungunya, and Gulu.
3. Hemorrhagic fevers: yellow fever, Philippine, Thai, Kyasanur Forest, Omsk, Crimean, and Argentinian.

Spectrum of Vectors

The spectrum of vectors of the arthropod-borne viral zoonoses includes mosquitoes of almost all genera, hard and soft ticks, phlebotomus or sand flies, and possibly mites. Mosquitoes transmit a majority of these viruses. Some tick vectors are capable of transmitting the viruses transovarially. The tickborne group includes Russian spring-summer encephalitis (RSSE), Kyasanur Forest fever, and Colorado tick fever. Mites have been incriminated on

epidemiologic evidence in the transmission of epidemic hemorrhagic fever of the Korean or Manchurian type. For some agents, the vector is unknown, but for most of these it will probably be found to be a mosquito.

Epidemiologic Patterns

The chart summarizes the epidemiologic patterns by illustrating the cycles recognized for a number of the arbo viruses. This information has been obtained through a great deal of careful field and laboratory research. Understanding these patterns is fundamental to understanding the distribution of these agents, the seasons in which the diseases occur, and the problems of control.

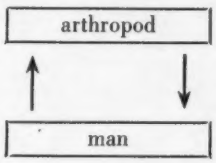
The first cycle requires viremia in the human host and an anthropophilic vector, usually a domestic one. Under these circumstances there can be transmission from man to an arthropod and then directly to other persons. This cycle is the most explosive type of disease progression among persons and leads usually to the epidemics with highest morbidity rates. Examples of these diseases are urban yellow fever, dengue, and phlebotomus fever.

The second cycle is much more complicated and may be basic to the first cycle. Many more diseases are in this latter group, which is a typical zoonosis pattern. The important vertebrate host is frequently a bird (cycle 2a), and the arthropod vector is one that feeds commonly on birds and only occasionally on man. Thus, the virus is maintained in nature, going from bird to vector to bird, but the vector occasionally bites man. If adequate viremia does not develop, man is a terminal host. If viremia does develop and there are anthropophilic domestic vectors, the first cycle described may continue. The typical members of this group, that is those in which man is an accidental or terminal host, include the well-known viruses of western encephalitis and eastern encephalitis.

Or the principal vertebrate host may be a lower mammal (cycle 2b). The result is essentially the same. Examples of this cycle are jungle yellow fever, Russian spring-summer encephalitis, Colorado tick fever, and others. In jungle yellow fever the vertebrate host is usually the monkey and the vector, a treetop mosquito,

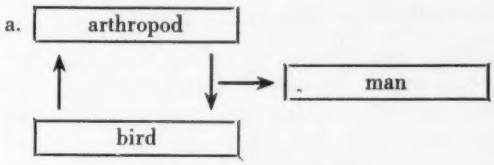
Epidemiologic patterns of arbo viruses and some of the diseases

Cycle 1: Adequate human viremia and anthropophilic vector:

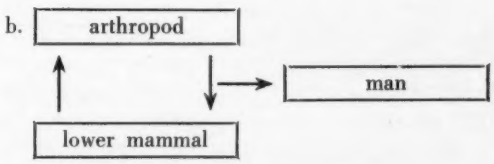


urban yellow fever, dengue, phlebotomus fever

Cycle 2: Inadequate human viremia or zoophilic vector, or both:



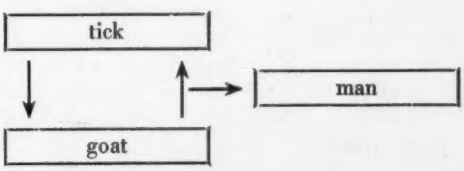
WE, EE, SLE, JBE



jungle yellow fever, RSSE, Colorado tick fever

Cycle 3: Combination of 1 and 2

Cycle 4: Milkborne:



diphasic meningo-encephalitis

while in Russian spring-summer encephalitis the vertebrate host is more frequently a rodent and the vector is a tick.

The third cycle is the complicated combination of cycles 1 and 2 and is excellently illustrated by jungle yellow fever and urban yellow fever. A man is bitten in the forest by a mosquito infected by a monkey, goes to the city at a time when he has viremia, local *Aedes aegypti* pick up the virus, and then the mosquito-to-man-to-mosquito-to-man cycle continues.

The fourth cycle, a modification of cycle 2b, is currently illustrated by only one virus. A tick infects a goat, but the virus is excreted in the goat's milk and man can be infected by drinking the milk. Explosive epidemics in man have occurred as a result of this type of transmission. The disease is called milkborne diphasic meningo-encephalitis in the U.S.S.R.

Determinants of Geographic Distribution

Means of introduction and maintenance determine the geographic distribution of the arthropod-borne viral zoonoses. A virus may be introduced where it has not existed previously by an infected man arriving in the area at a time when he develops viremia. The virus can thus be picked up by local vectors. In this fashion yellow fever and dengue, for example, have been introduced many times in years past in coastal cities of the United States. Or introduction can occur by importation of a vertebrate, other than man, with viremia, or by importation of infected arthropods by plane, boat, train, or automobile. All these events have probably served as methods of introduction of viruses in the past.

In addition to transportation by man or in his vehicles, the migration of infected birds is another distinct possibility as a means of introduction which has received much attention in recent years. A bird may be infected in an endemic area, fly for great distances during migration, and arrive in an area free from the virus, but viremia in the bird serves as a source of infection for local vectors. Another potential source, in addition to the viremic bird, is minute infected vectors carried in a bird's feathers. These vectors may transfer to local birds, thus serving as the means to implant the new virus.

After introduction of the virus there must be means for maintenance. In the first situation, there is a suitable, year-round vector present in abundance and an adequate number of susceptible, potentially viremic hosts so that the virus cycle may continue throughout the year. These requirements are met most frequently in the tropics, and under these circumstances, there is no difficulty in understanding how the virus may maintain itself. However, in temperate zones where the vector or vector's activity is only seasonal, although there are adequate numbers of potentially viremic hosts in the area, some special mechanism must exist for carrying the virus through the winter season when the vectors are not normally active and biting.

A great deal of research has been devoted to seeking this mechanism for several viruses during the past 15 to 20 years without obtaining definitive answers. Western, St. Louis, and eastern encephalitis, as they occur in this country, are examples of this difficulty as is Japanese B encephalitis in the Far East. Considered and studied intensively as possibilities are hibernation of infected vectors, transovarian infection, and latent infection in birds, snakes, or other vertebrates, with viremia appearing in the spring or early summer at the time that the mosquito vectors become available. If there is no suitable method for carrying the virus through the winter in a reservoir in a particular area, the virus disappears until it is reintroduced during the vector season by one of the means described previously. In addition to the viruses already mentioned, dengue and yellow fever may be maintained in the coastal areas of the United States by such mechanisms. It has been suggested that eastern encephalitis is being reintroduced into coastal areas of eastern United States by birds migrating from the south or by some other as yet unknown mechanism.

Currently Recognized World Distribution

I shall discuss the recognized distribution of the arbo viruses very briefly, partly because the information is changing so rapidly that current knowledge will be completely out of date within 1 or 2 years.

We can state rather clearly that these viruses are transmitted only in parts of the world where

there is a season of warmth adequate for vector development and for intrinsic incubation of the virus in the vector. These viruses will not multiply in the vector unless the temperature remains above certain levels. At the lower minimum levels, the incubation period is prolonged and, therefore, the likelihood of repeated cycles of infection is minimal. For this reason, the Arctic areas are essentially excluded from the distribution pattern.

In this hemisphere members of this group of viruses are recognized from southern Canada to the tip of South America. Viruses have been recognized from Scotland, Scandinavia, European U.S.S.R., to the southern tip of Africa. In the Far Eastern areas viruses are recognized in the maritime provinces of the U.S.S.R., Korea, and Siberia to the southern tip of India. In the Pacific, they are recognized in the Japanese islands, the Ryukyus, the Philippines, the Marianas, Indonesia, Australia, and New Zealand. In short, the world is pretty well covered except for the Arctic areas.

I do not mean to imply, however, that these viruses are evenly distributed. There are many localities where they have not been introduced or where suitable vector or vertebrate hosts are not present. Such areas are apparently entirely free from any of these agents. Therefore, the distribution of the arbo viruses is spotty and varies greatly from the distribution of such viruses as measles, influenza, and poliomyelitis which exist where there are human hosts and travel, for vectors and other vertebrate hosts are not essential in their cycle.

Number of Viruses

The number of viruses in the arthropod-borne group which are now recognized and studied adequately enough to determine that each is a distinct entity is probably near 150. The number increases almost weekly. Those known to produce disease in man are fewer; my estimate of these at the moment would be about 50.

Antibody studies, however, reveal that many more infect man, but their disease potential has not yet been determined. Because of the crossing of antibodies between certain of these viruses, it cannot be determined with certainty at present whether detected antibodies for a certain virus means infection with that virus or with another closely related to it. This is another reason why it is difficult to give an accurate number of those which infect man. Undoubtedly, the number of agents in this group is tremendous, and in my opinion, will turn out to be one of the largest and most complex groups of viruses existing in the world. Young virologists, epidemiologists, and others who are searching for a fruitful area of research and discovery should consider the opportunities in investigations of these viruses.

Prevention and Control

For most members of this large group of agents, at present there is no organized method of control. Discussion, therefore, is limited largely to the principles of potential control.

Under certain circumstances vector control is the most logical and practical preventive measure for some agents. Its effectiveness has been well established for yellow fever and dengue in urban areas through the eradication of *Aedes aegypti* mosquitoes. Control of *Culex tarsalis*, the principal vector of western encephalitis and St. Louis encephalitis in the San Joaquin Valley of California, has been attempted for a number of years, in part resulting from the stimulation of our studies. *C. tarsalis* has protean breeding habits, and a great deal of research has gone into the study of its ecology. Control methods have been developed which are generally practical but expensive. Nevertheless, endemicity in the valley is of sufficient importance that control has become imperative. Reeves and I recently summarized the evidence of the effectiveness of this control in a monograph now in press, covering studies carried out from 1943 through 1952. We consider that the evidence is adequate to indicate that vector control has had a definite effect in reducing the incidence of human disease.

For many years the Russians have carried out some degree of control on vectors of the Russian spring-summer tickborne group of viruses in certain endemic forest areas. This is most difficult and expensive, but in their experience these measures are justified.

Artificial immunization of human populations against these viruses is in its infancy. Both active and passive immunization have been considered.

Active immunization with a live attenuated viral agent has proved highly effective for yellow fever. As the only practical method in jungle areas, it is widely applied to travelers entering and departing from recognized endemic areas. In the experimental stage are several other attenuated viral agents for human use which look quite promising. They include Venezuelan encephalitis virus and Rift Valley fever virus. We have in the laboratory of the University of Pittsburgh Graduate School of Public Health at the present time an attenuated strain of Japanese B encephalitis virus, the result of several years of effort to obtain attenuation of an adequate degree. We are almost ready to undertake limited human trials with this strain.

Several formalin-inactivated virus vaccines have had extensive field trials, some apparently with reasonable success. The Russians for many years have employed a formalinized mouse brain vaccine for the Russian spring-summer encephalitis virus, apparently with considerable success. But the protection it offers is limited, and its use has not been free from accidents because of sensitization with central nervous system tissues from the mouse brain. Russian scientists are currently exploring inactivated tissue culture preparations. Our military services used an inactivated mouse brain or chick embryo vaccine for Japanese B encephalitis for several years but abandoned this practice because the degree of effectiveness was not that expected. Formalin-treated chick embryo vaccines for western, eastern, and Venezuelan encephalitis viruses have been used extensively and with apparent success in horses.

During recent years evidence obtained by many of us concerning cross immunity produced by certain viruses to others within the same immunological group lends a certain amount of optimism to prospects for control by active artificial immunization, particularly with the live attenuated viral agents. There is some evidence, for example, that the new attenuated Venezuelan virus vaccine will produce in horses immunity not only to the homologous virus but also to western and eastern encephalitis viruses. In laboratory animals we have shown that immunization to one or two members of Casals' group B viruses with live virus will provide at least a moderate degree of protection against several others in the same immunological group. If the live virus immunization is supplemented with one or two injections of killed virus vaccine prepared from another member of the group, the breadth of immunity is extended still further.

Passive immunization with gamma globulin from immune individuals or from hyperimmune animal serums has proved effective in laboratory animals and is frequently used for accidents occurring among laboratory workers. Certainly, there are instances in which its use is justified. It has never been evaluated for large-scale use, and the short period of protection offered by such immunization makes it unlikely that it will find many fields of practical application.

Control of the transportation of these viruses by air, land, or sea vehicles has been attempted. Some international measures now required are not adequately enforced, and some methods employed are relatively ineffective. With the possible exception of yellow fever vaccine for man, there is little control, or even attempted control, of the movement or shipment of potentially infected vertebrates including man. Much more research is required before there can be an extension of this type of control to other viruses in the group.

At present there is no obvious way of controlling the flight of birds which are infected and viremic, or the possible vectors which they may carry. More data concerning this could be acquired, but even with such knowledge effective control appears unlikely.

SYMPOSIUM ON WORLD MEDICINE

The Future of Immunization

GEOFFREY EDSALL, M.D.

EVER SINCE Jenner established the principle of vaccination more than a century and a half ago, immunization has been the most efficient method ever devised for protecting men and animals from disease. Under ideal conditions, it converts a susceptible man to a resistant man, enabling him to move wherever he chooses, whenever he chooses, carrying his protection with him. Unlike chemoprophylaxis, immunization frees him from having to take a drug regularly, with the risk of running out of the supply of the drug or the mental hazard of forgetting to use it. Unlike water sanitation or insect control, immunization permits him to leave a protected area without leaving his protection behind him. And no longer must he periodically flee an epidemic area, hoping that he has left in time.

Gains such as these, unparalleled in preventive medicine, have saved millions of lives and freed other millions from panic or from chronic fear. But few immunizing procedures approach this ideal. Even smallpox vaccination does not provide lifetime protection (as Jenner first thought), and most other immunizing procedures, with the probable exception of yellow fever vaccination, appear to be limited in the duration of their efficacy. More serious is the imperfect degree of protection afforded by the majority of vaccines. In addition to smallpox and yellow fever vaccines, only one other virus vaccine is strikingly effective, poliovirus vaccine.

We have an excellent bacterial vaccine against whooping cough, a relatively good one against tuberculosis, and a moderately effective one against typhoid fever; remarkably effective toxoids against diphtheria and tetanus; highly effective but now obsolete polysaccharide antigens against pneumococcus infections; vaccines against typhus fever and Rocky Mountain spotted fever, both considered very useful but not in the same class as yellow fever vaccine; and moderately good virus vaccines against influenza and rabies. Aside from certain specialized vaccines such as those for tularemia, brucellosis, and adult adenovirus infections, and those now under development like measles vaccine, this list is virtually complete except for a series of preparations the usefulness of which is hard to establish: vaccines against cholera, plague, mumps, paratyphoid fever, staphylococcus infections, and the like.

When one considers the well-known limitations of these agents and the list of infectious diseases for which no really useful vaccination procedure is available, the record is far from satisfactory, and it is difficult to agree with the statement recently credited to Sir Macfarlane Burnet (*1*) that "today the technique of immunization provides protection against all the significant diseases that have not been eliminated by public health measures or that do not yield readily to chemotherapy." The fact is that there are still great deficiencies in our knowledge of both the principles and the application of immunization. Nevertheless, there are many good reasons to believe that major progress can be achieved to remedy these deficiencies in the future.

But one may ask, Is this the major path to follow? With the tremendous, continuing advances in antibiotic therapy, with the prospect of steadily increasing sanitation extending throughout the world, and in view of the diffi-

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culties that have beset past efforts to immunize against many infectious diseases, is a major effort to continue the extended application of immunology to control infectious diseases justified? Or should one take the position that the easy problems in immunization have been solved, and that the difficult ones will either be insoluble or will be solved more readily by other approaches?

Let us first consider immunization as we see it today. Surely little doubt exists of the lasting usefulness of smallpox vaccine, pertussis vaccine, diphtheria and tetanus toxoids, yellow fever, rabies, poliovirus, measles, influenza, adenovirus, and perhaps certain other vaccines. For many years we will need typhoid and BCG vaccines and a large measure of faith in cholera and, in certain limited areas, plague and typhus vaccines. No matter what chemotherapeutic magic may arise, the essential simplicity of prevention by immunization will give it value wherever prevention by other means is less than wholly effective.

Indeed, one may expect that certain immunization practices will be continued indefinitely. To be sure, the eradication approach may eventually solve some current problems. However, even in such a promising instance as smallpox one can reasonably assume that for many years there will remain small isolated groups of people, in areas difficult of access, where smallpox will persist and constitute a recurring threat to the rest of the world.

Clearly, however, we could protect against many additional diseases by immunization if adequate methods were available, especially for those infections for which no convenient, practical alternative means of control is in sight. Yet the problems are multiple. Many unsolved difficulties in disease control revolve around what appear to be basic deficiencies in the antigenic response to the disease, and others are complicated by the multiplicity of antigens concerned. Certainly no single line of research promises success, for on the one hand the patterns of immunity in nature differ tremendously from disease to disease, and on the other hand the specific immunizing antigens in various diseases differ greatly in chemical composition, stability, ease of extraction and purification, and, indeed, in antigenicity. Finally, the various diseases which concern us differ among themselves in their basic antigenic stability. Contrast, for example, mumps, which clearly has not changed much since the days of Hippocrates, with influenza for which the best we can say is that it hasn't changed much during the last 3 years.

Each disease is a problem in itself, and blueprints for progress will be hard to come by even at a high price. Nevertheless, it is worth the price to try to develop these blueprints; for never in the history of human progress has a better and cheaper method of preventing illness been developed than immunization at its best. In this spirit, it appears worthwhile to define the difficulties that might conceivably be solved by immunological methods and principles.

What Is Needed

To sharpen the focus, one might start with a list of the disease conditions for which progress in immunization is most needed. Such a list might read as follows.

1. A better vaccine against tuberculosis. BCG is a good vaccine but it is not good enough. A more effective and less reactive vaccine would gain wider acceptance and will be urgently needed if, as may well happen in the next few years, drug resistance outruns the capacity to devise new chemotherapeutic agents that are safe, effective, and readily used on a large scale.

2. An effective vaccine against hemolytic streptococcal infections, or at least against the types most responsible for serious sequelae. Chemoprophylaxis of the complications of streptococcal infections represents a great advance; but it is less than satisfactory to be obliged not only to grab the hose, so to speak, after the chimney catches fire, but then to continue sprinkling the chimney regularly for the next 5 years to prevent flareups.

3. Effective combinations or sequences of immunization against the prevailing upper respiratory infections. This will require great patience and ingenuity, for here the immunologist is challenged to develop the necessary basic understanding of the immune response and the factors which enhance or modify its course, so that he can evoke the requisite mosaic of ade-

quate immune responses to the great variety of respiratory disease agents involved.

4. A durable yet rapidly adaptable system for vaccination against influenza. The problems here are different, notably because of the race against time that ensues when a new strain appears. But we must assume that technical advances can be developed which will surmount such obstacles. I believe that when the next major pandemic occurs we should be able to immunize all except those who are overtaken by the virus within the first few weeks of its emergence.

5. A vaccine or vaccines against the major diarrheas and dysenteries. These infections are as complex as those of the acute respiratory diseases, and equally important. Ultimately, they will be solved by sanitary engineering techniques, but it will be a long time before the people in the areas most affected by these diseases can afford to bring them under control by these methods.

6. An improved vaccine against cholera, needed now for the same reasons.

7. A vaccine against scrub typhus. Area control and chemoprophylaxis may not be adequate for protection of persons pioneering in the development of scrub-infested regions; although immunization in this instance is an especially formidable task, there are potential immunological approaches which have not yet been tried.

8. Better vaccines against several of the more serious arthropod-borne viruses, such as Japanese encephalitis, Russian spring-summer encephalitis, and Kyasanur Forest disease. Development of such vaccines may in turn open the way for the control of the denguelike diseases, and analogous conditions for which control of arthropods will not always be feasible.

9. A vaccine against trachoma. The need is obvious; the problem is difficult; but as I have said, the easy problems have already been solved.

10. A vaccine against the more serious or persistent staphylococcal infections. With these more than with any other infections, the cozy glow of comfort created by the advent of the antibiotics has died out, and the ensuing chill of reality has sent many investigators back to basic immunological studies.

11. A procedure for immunization against hepatitis, granting, of course, the prior assumption of success in isolating the causative agent or agents.

12. Vaccines for control of the so-called minor exanthems, such as varicella and rubella, which, minor though they have long appeared, nevertheless have occasional tragic consequences.

13. We cannot afford to forget the need for seeking effective means of immunization against the major parasitic diseases, trypanosomiasis, schistosomiasis, and malaria. Eventually, all may be subject to area control, but this result is by no means certain; and recent setbacks in the control mechanisms for malaria justify a reexamination of the supposedly insuperable task of immunological protection against this disease.

14. In certain parts of the world, brucellosis will not be eliminated by sanitary measures for many years, and the presently available vaccines are less effective and more reactive than could be desired.

15. Immunization against some zoonoses that I have not mentioned will be important in certain regions of the world, but far more necessary are really effective vaccines against the epizootic diseases that seriously threaten the food supply of major areas of the world: rinderpest, anthrax, African horse sickness, hog cholera, fowl cholera, and others.

16. Control of the allergies has for years been handled as a variant of the principle of immunization, yet this problem is far from solved. Again, further progress in fundamental immunology, already well underway, needs to be sustained in order to reach the goals that now begin to appear attainable.

17. Perhaps equally urgent is the need to develop means of controlling or mitigating so-called delayed or "bacterial" allergy, an aspect of the immune response which is not merely responsible for many reactions to immunization but also appears to play a major role as a cause of persisting symptoms or complications in many chronic infections.

18. Finally, there is growing reason to believe that immunological means may be developed for the control of some, though perhaps by no means all, varieties of cancer and other malig-

nant diseases. This prospect alone will suffice to mobilize the greatest talents in immunology, and it is certain that more than one basic approach will have to be explored.

Some will regard this list as inordinately optimistic; others may consider it incomplete. However, it is offered primarily as a basis for discussion and review and as an incentive to new and uninhibited intellectual and scientific adventure. We cannot afford to be bound by the conviction that we know all about the immunological approaches to any of these diseases and conditions, and we may be sure that even less familiar questions will arise in the future.

Additional Considerations

Nor can we sum up the problems of immunization simply with a hopeful list of diseases to be conquered. There are many more general questions to be solved. For example, what will be the role of adjuvants in immunization? The modified Freund adjuvant has been used in perhaps 80,000 to 90,000 inoculations in man. Yet we have relatively little knowledge of its long-term effects. These effects are probably few and may well be insignificant, but we cannot be content to guess the answers to such questions. In any case, the development of an effective and practical adjuvant system demands top priority if multiple immunizations are to be carried out effectively on a large and long-term scale.

Equally needed is clarification of the fundamental stages in the process of inducing an immune response. The development of such knowledge may, at best, show the way to major changes in the entire sequence of immunization procedures; it should at least bring some order out of the present empirical chaos of immunization schedules in which the dose, the interval between injections, the number of injections, and the timing of (or even the need for) booster doses are as varied as the people who write or speak on this subject. Also, we need to find ways to accelerate the primary immune response. An adequate technique for inducing rapid immunization against tetanus, for example, might conceivably do away with the present wasteful and sometimes harmful procedure of prophylactic tetanus antitoxin inoculation.

Studies in the institute of laboratories are being directed to several of these needs, and a number of my fellow immunologists are engaged in basic studies that may yield the necessary breakthroughs in these principles of immunization. But sufficient talent has not yet been enlisted in this task, and those engaged in it must be given every opportunity to develop the knowledge and skills of those who may choose to enter the field. The solution of the problems I have described has far more than theoretical importance; the establishment of simplified, effective immunization schedules may in itself mean the difference between success and failure in applying immunization in developing countries where health departments are understaffed and the populations cannot be reached for the multiple injections customary in the Western World.

Because only the difficult problems remain, there is now a greater need than ever before to support research and to encourage research workers in fundamental microbiology and immunology. Immunology is still far from an exact science, but it is capable of providing some fairly precise information. When we understand more, for example, about the apparent poverty of the immune mechanism in tuberculosis or malaria, more about the genetics of influenzal strain variations, and more about the role of microbial allergy in trachoma, we will then be in a position to undertake control of these diseases more rationally and will be less dependent on luck, serendipity, and a level of patience that is sometimes hard to sustain.

The solution of immunological problems encompasses a variety of scientific disciplines. We are indebted largely to biochemistry and biophysics for the relatively pure toxoids currently available, for the quality and stability of most of the gamma globulin in use, and for the potency and freedom from extraneous substances of the purified poliovirus vaccine recently developed. But no immunization procedures yet developed have equaled those based on the virological luck and skill which led to the establishment of safe, attenuated vaccine strains such as the 17D strain of yellow fever virus. Such attenuated live vaccines generally establish lasting immunity by producing a mild form of the infection itself.

Nevertheless, for some diseases the major breakthrough will come through immunochemical and immunophysical separation, purification, analysis, and eventually even synthesis of the specific substances which initiate the immune response. Others may be met by unraveling the specialized cellular pathways to immunity which appear to be of major importance in many subacute and chronic diseases. Along other lines of investigation we might find, in serum hepatitis, for example, that the virus circulates largely in the raw nucleic acid form. Will it be possible, in such instances, to prevent the disease by immunizing against the nucleic acid core?

Still other mechanisms important to specific immunity are yet to be discovered. We think only in terms of what we know, and inevitably new concepts and discoveries will arise in the future, as new and unexpected as vaccinia virus and diphtheria toxoid were in their day.

There is more to immunity than specific immunity. Many species or strain differences in susceptibility to specific infectious agents fascinate and baffle us. These problems may gradually be solved as knowledge of the precise biochemical processes of infection becomes clarified through the development of experimental studies capable of testing specific and interpretable postulates. In addition, research into nonspecific resistance of the individual host to its own natural parasites is still in the embryonic stage. The hopes engendered a few years ago by the late Dr. Louis Pillemer's brilliant studies on properdin have not been wholly sustained, but they represent an area of research which will be rekindled again, since there is extensive evidence, accumulated over many years, that there are factors in animal serums responsible for significant resistance in its broadest rather than in its conventional narrow sense. The discovery by Isaacs and his colleagues of "interferon" is an exciting example of the unpredictable ways in which this whole area of research may advance at any time.

Consequences of Immunization

However, we rarely get something for nothing, and we cannot ignore the different set of problems which may be engendered by multiple, repeated immunizations or by other aspects of this process, which is based upon the rather violent procedure of introducing foreign substances into the body. The problem of delayed-type bacterial allergy has been mentioned; there is growing evidence that cumulative sensitization even to tetanus toxoid occurs, and some immunizations are definitely associated with a progressively increasing hyper-reactivity on reinjection. This phenomenon may mount in the future; I believe our only assurance, once again, will be in research on the basic mechanisms underlying immunization and sensitization. These two phenomena may or may not go hand in hand, but we must find out to what extent they are interdependent. A positive tuberculin test appears to be an inescapable consequence of tuberculous infection, but a positive Moloney test is not an inevitable accompaniment to diphtheria immunity. Observations such as these may serve as the directional signals to useful pathways of research.

Other consequences of immunization may be more serious than the reactions I have just mentioned. Aside from the specialized difficulties raised by special techniques—for example, the questions of possible sensitization to kidney tissue from use of monkey kidney tissue culture vaccines or the possibility of inoculating tumor-inducing chromosomal material along with antigens grown in primate tissue—other, more general problems may conceivably follow the injection of foreign substances into man. There is reasonable evidence that certain auto-immune responses may result from the conjugation of "foreign" antigens with host antigens, to cite one example, and we are again reminded that we know too little about the sequence of events that follows the injection of heterologous antigens. The definition of "heterologous" becomes more and more difficult with the recent succession of discoveries suggesting forcefully that each human being may share the complex antigenic mosaic pattern of his tissues with only a few other men on earth.

None of these thoughts need deter the development and application of immunization practices, but they point up once again the paramount importance of fostering, at an equal pace, the support of basic research in immunology and hypersensitivity.

One cannot deal with immunization without considering its obverse, immunological tolerance. Understanding of one underpins understanding of the other. With a better understanding of immunological tolerance and how it is induced or controlled, a host of preventive and therapeutic approaches to surgical, radiological, oncologic, and infectious disease problems will be open to solution.

Other Needs

Of certain other aspects of the future of immunization there is no need to speculate; the facts are clear. We must now be prepared to accept no half-truths in immunization. We must correctly determine the value for man of the agents now in use and those to be provided in the future, through controlled field trials which yield statistically significant and biologically acceptable data. For too many years we have been content to base acceptance of immunization procedures on relatively raw data in man or on superbly precise studies in mice, or sometimes on nothing much more than wishful thinking. Let us take as a standard the well-known critical evaluations, by controlled field trials, of pertussis, influenza, tuberculosis, and poliomyelitis vaccines, and, on a smaller scale, those of adenovirus, typhoid, and measles vaccines. May the number of vaccines legitimized in this fashion steadily increase.

Vaccination presents sociologic as well as scientific problems. It will do little for the future of immunization to prepare excellent vaccines, test them to a fare-thee-well for safety and efficacy, and then not insure that they are adequately used. We become steadily more impatient as we see science, in this instance as in so many others, outrunning society. I am deeply convinced that a paramount problem in immunization in the future, and one for which we must all share responsibility, is to get vaccines into the people who need them. In a country as civilized as the United States it is shocking to find that about 20 percent of the youth 15–19 years old and about 40 percent of the young adults 20–29 years old have never had a single injection of poliovirus vaccine. Immunization programs in the developing countries will present similar challenges. They will require not only basic research on the patterns of effective immunization but skilled planning and courageous action to carry through the indicated procedures on an effective scale, and thus to reach the population groups most in need of protection. However, the developing countries may have one real advantage: they can learn from our mistakes.

Summary

I believe it is fair to say that immunization, while not exactly in its infancy, is scarcely beyond early childhood; that advances in immunization must depend upon vigorous development of knowledge in basic immunology; that, as in other scientific disciplines, major breakthroughs are expected to occur, and that they will, in all probability, occur in unexpected, unforeseen ways. Moreover, these breakthroughs will unquestionably be applicable not only to infectious disease and to allergy in the conventional sense but also to isoallergic disease, tumors, radiological injury, surgical problems, congenital diseases, certain degenerative diseases, and perhaps to other categories, such as geriatric diseases.

Finally, scientific philosophy and intellectual humility must always keep us prepared to see the adverse as well as the advantageous consequences of our actions. Nevertheless, immunization still represents, in principle, the most fortunate discovery ever made in the advancement of human life and health, and its continued fulfillment will proceed in proportion to the brains, talent, and imagination that are devoted to its future.

REFERENCE

(*1*) Burnet, M.: The mechanism of immunity. Scient. Am. 204: 58–67, January 1961.

Occupations of Men Dying From Accidents in the United States, 1950

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FATAL ACCIDENTS accounted for more than 10 percent of the deaths included in the National Vital Statistics Division study of mortality for 1950 by occupation and industry among men 20–64 years of age. Of the 327,271 deaths recorded, 34,949 were reported to be due to accidents, 8,297 at work and 26,652 away from work and unspecified. The death rates per 100,000 men for both types of accidents reached a peak at the older ages. The figures for each age group are shown in table 1.

When the difference in ages of the men in each occupation and industry is taken into account, the rate for work accidents among lumbermen was eight times the average for work accidents among all men, and among mine workers and structural metal workers, more than five times the average. By industry, the same high risks were reflected in the rate for logging, which was 10 times the average, and for coal mining, which was almost 5 times the average. The range of death rates by occupation or industry was much narrower for accidental deaths that were not described as taking place at work.

Nature of Data

A copy of each death certificate filed in State vital statistics offices is sent routinely to the National Vital Statistics Division, where data are compiled for the United States. Deaths in 1950 were classified in the National Vital Statistics Division by the "usual" occupation and industry—the kind of work done during most of life—reported on the death certificate, as well as by age and cause of death. These figures, along with the count of the current occupation of the population by age as enumerated in the census of population for April 1950, made it possible to compute age-specific and age-adjusted death rates for each occupation, for each industry, and for groups of occupations or industries.

The numbers of deaths from accidents and the standardized mortality ratios assigned to the major occupation and major industry groups are shown in table 2. The standardized mortality ratios also appear in figures 1 and 2. The standardized mortality ratio is the number of deaths tabulated in each occupation or industry group divided by the number that would have been expected if the age-specific death rates in the occupation or industry were the same as those rates by age shown in table 1.

The major occupation and industry groups have been established by the Bureau of the Census (*1*) and are designed to bring together occupations with the same type of work and industries with related processes. In this paper, two of the census occupation groups, farmers and farm laborers, have been combined because the distinction between them is based on the question concerning class of work—whether working for private employer, in own business, and so on—which appears on the census schedule but not on the death certificate. Also, the small number of private household workers has been combined with other service workers.

Interpretation of Data

A standardized mortality ratio significantly above 100 for a particular occupation should indicate an unusual risk of death from accidents

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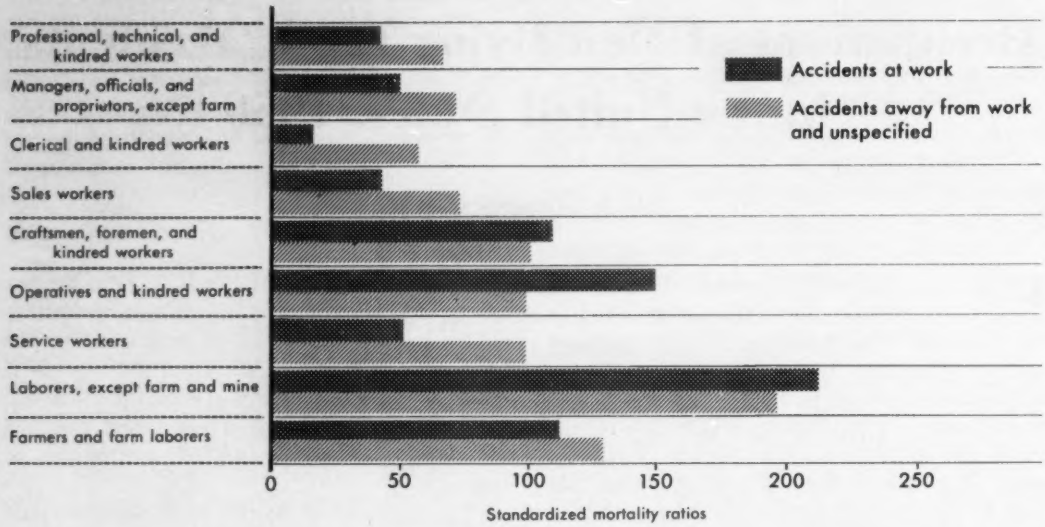
Figure 1. Standardized mortality ratios for accidents in major occupation groups, men 20–64 years of age, United States, 1950



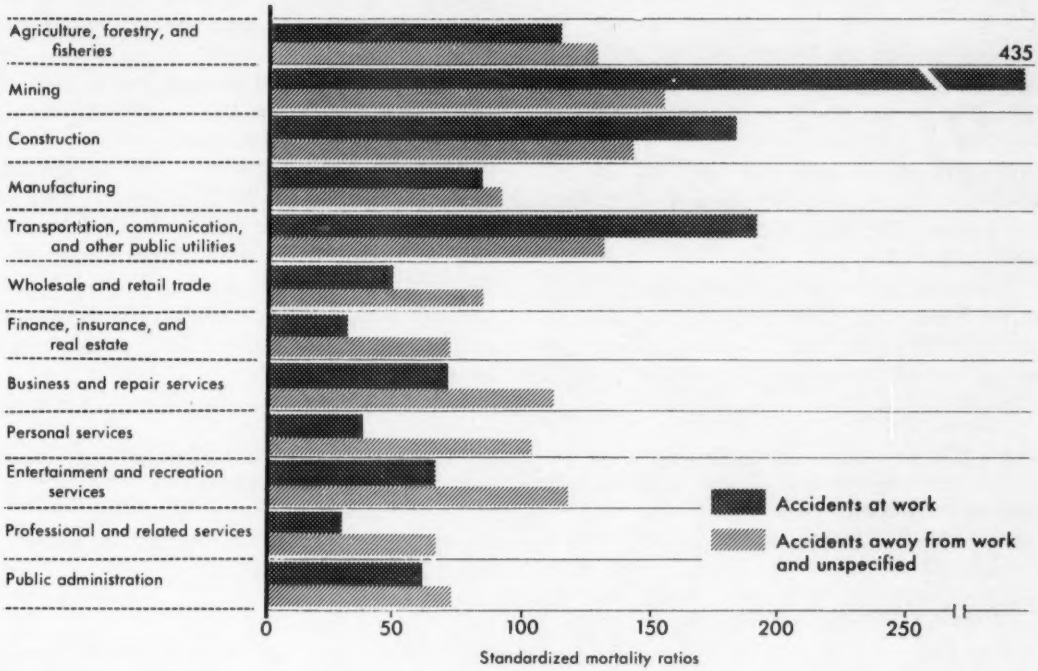
for men working in that occupation or industry. But a high ratio for any cause can occur as well from an overstatement of the number of persons in the occupation or industry reported on the death record in comparison with the reports of the number in the same occupation or industry in the census. Occupation and industry are difficult items to report precisely, both for deaths and for the enumerated population. A comparison of the occupation of an individual reported on the death certificate with the occupation reported for the same individual on the census schedule was made by the Scripps Foundation for Research in Population Problems for white males 45–64 years of age who died after the date of the census of 1950 (*2*). The study showed that 70 percent of these persons were reported in the same major occupation group and 80 percent in the same major industry group on both death certificate and census schedule. The net distribution of major occupation groups from the two records differed significantly for three groups only—clerical, craftsmen, and operatives.

These findings may not apply to an occupation or industry that is subject to systematic errors in reporting, either on the death certificate or on the census record, which may result in an understatement or overstatement of death rates. The effect of such errors can be eliminated by comparing the proportionate mortality ratio—the number of deaths from accidents per 1,000 deaths from all causes—for an occupation with the proportionate mortality ratio for all occupations, since this involves no use of the census data. This approach was suggested by Dr. Percy Stocks in his review of the occupational data for the United States as consultant to the Public Health Service, assigned by the World Health Organization.

Table 1. Deaths and death rates from accidents, men aged 20–64 years, United States, 1950, by age group and work status

Age (years)	Number of deaths		Rate per 100,000 population	
	Not at work and unspecified	At work	Not at work and unspecified	At work
20–64	26, 652	8, 297	66. 3	20. 6
20–24	3, 830	907	84. 6	20. 0
25–29	3, 301	974	61. 0	18. 0
30–34	2, 854	969	54. 0	18. 3
35–44	5, 784	2, 007	56. 7	19. 7
45–54	5, 371	1, 834	64. 2	21. 9
55–59	2, 825	873	80. 7	24. 9
60–64	2, 687	733	91. 3	24. 9

Figure 2. Standardized mortality ratios for accidents in major industry groups, men 20–64 years of age, United States, 1950



If the proportionate mortality ratio for accidents is significantly higher for a particular occupation than this ratio for all occupations, it may be because the risk of accidental death for workers in that occupation exceeds the risk for all occupations. If the standardized mortality ratio is also high, then the risk of accidental death is in fact great for men reported as working in that occupation or industry compared with the risk for the male population as a whole. If the proportionate mortality ratio is not higher than expected, in spite of a high standardized mortality ratio, the latter may be the result of an overstatement of deaths for the occupation or industry in relation to the population enumerated in this occupation or industry or of high nonspecific mortality for the entire occupation or industry. A choice between these explanations cannot be made from the information at hand.

In any case, when a high risk of deaths from accidents is confirmed by a high proportionate mortality ratio it should be remembered that the figures presented are for the mortality experience of a group of persons in a particular occupation or industry. The risks described may arise from selection of persons drawn into an occupation and the social and economic conditions associated with the occupation, as well as from hazards in the occupation itself.

Before either the standardized mortality ratio or the proportionate mortality ratio was computed, estimates of the occupational distribution of deaths for which no occupation was reported were included in the base figures, as well as estimates of the distribution of the retired population by occupation and industry. The estimating procedures are described in a report now in preparation (*3*).

Accidents at Work

In this paper the division of accidents into those occurring at work and those not occurring at work has been made according to information given on the death certificate. If "Injury occurred while at work" (item 20d, Standard Certificate of Death) was not checked, the acci-

dent was included with the group occurring "away from work and not stated."

Occupation

From figure 1 it is evident that the standardized mortality ratio for accidents while at work is extremely low for professional, managerial, clerical, sales, and service workers. The standardized mortality ratio was above average for craftsmen, operatives, and laborers. The ratio for farmers and farm laborers was about the same as for craftsmen.

The total number of accidental deaths while at work is so small that a meaningful standardized mortality ratio cannot be computed for each occupation of the Intermediate List of Occupations (*1*). Computations were limited to classes for which more than 20 deaths were reported for this cause. However, among these occupations there are many groups for which the frequency of accidental death is far beyond the expected value.

From the nature of their work, few accidental deaths would be expected among "professional, technical, and kindred workers." More than 20 deaths are reported for only two occupation classes in this group—civil engineers, with 22 deaths assigned and a standardized mortality ratio of 88, and the residual group, "other professional, technical, and kindred workers," with 119 deaths and a standardized mortality ratio of 118, not significantly above the average for all occupations.

More than 20 deaths were recorded for work

Table 2. Deaths from all causes and from accidents, and standardized mortality ratios for men 20–64 years of age, by major occupation and industry group, United States, 1950

Major occupation or industry group	Number of deaths			Standardized mortality ratios		
	All causes	Accidents		All causes	Accidents	
		While at work	Away from work and unspecified		While at work	Away from work and unspecified
Men in all occupations and industries, aged 20–64 years	327, 271	8, 297	26, 652	100	100	100
Occupation						
Professional, technical, and kindred workers	19, 087	249	1, 250	88	42	66
Managers, officials, and proprietors, except farm	37, 628	451	2, 069	89	49	73
Clerical and kindred workers	15, 188	79	918	84	15	55
Sales workers	16, 834	214	1, 169	96	44	74
Craftsmen, foremen, and kindred workers	65, 119	1, 756	5, 126	99	108	100
Operatives and kindred workers	55, 086	2, 535	5, 445	96	149	98
Service workers, including private household workers	26, 715	251	1, 542	116	52	98
Laborers, except farm and mine	43, 772	1, 508	4, 579	163	212	196
Farmers and farm laborers	47, 842	1, 254	4, 554	96	112	126
Industry						
Agriculture, forestry, and fisheries	50, 130	1, 357	4, 827	97	116	128
Mining	10, 424	905	1, 029	125	435	154
Construction	35, 837	1, 371	3, 397	118	181	140
Manufacturing	77, 200	1, 781	6, 361	93	79	88
Transportation, communication, and other public utilities	38, 695	1, 495	3, 241	123	190	128
Wholesale and retail trade	52, 199	656	3, 615	99	47	80
Finance, insurance, and real estate	9, 702	73	493	97	33	70
Business and repair services	9, 257	176	893	109	70	110
Personal services	12, 119	86	771	116	37	104
Entertainment and recreation services	3, 770	54	302	133	69	118
Professional and related services	13, 503	112	833	83	29	68
Public administration	14, 435	231	890	96	61	74

accidents in each of four classes within the major occupation group "managers, officials, and proprietors," but in each case the standardized mortality ratio was below average. Several occupation classes among "clerical and kindred workers" and "sales workers" averaged more than 20 deaths from work accidents, but the standardized mortality ratio was extremely low for every class.

Among "service workers" the standardized mortality ratio for work accidents was above average, but not significantly so, for "policemen, sheriffs, and marshals" only. Since the standardized mortality ratio for accidents occurring at work is no higher for this group than this ratio for all causes for policemen, the proportion of deaths assigned to work accidents was not higher than expected. It would require other information to establish clearly that the risk of death from accidents was excessive for policemen.

The remaining major occupation groups each contain several occupations with high mortality from work accidents. The proportionate mortality ratio as well as the standardized mortality ratio was computed for each occupation in the Intermediate List (*1*). When both ratios are high there can be little doubt that an excess risk existed in 1950. These occupations, the numbers of deaths, and the standardized mortality ratios are shown in table 3.

Table 3. Deaths from accidents occurring at work and standardized mortality ratios, for selected occupations and industries,[1] men 20–64 years of age, United States, 1950

Occupation or industry	Number of deaths	Standardized mortality ratio
Occupation		
Farmers and farm laborers	1, 254	112
Cranemen, hoistmen, and construction machinery operators	123	273
Electricians	155	231
Foremen (n.e.c.), nonmanufacturing industries	114	168
Linemen and servicemen—telegraph, telephone, and power	180	429
Locomotive firemen	26	236
Millwrights	27	225
Stationary engineers	80	178
Structural metal workers	61	555
Brakemen and switchmen, railroad	106	353
Mine operatives and laborers (n.e.c.)	726	581
Truck drivers and deliverymen	938	293
Other specified operatives and kindred workers	97	243
Operatives and kindred workers (n.e.c.): sawmills, planing mills, and miscellaneous wood products	59	179
Fishermen and oystermen	38	271
Lumbermen, raftsmen, and wood choppers	304	844
Laborers (n.e.c.), construction	392	260
Industry		
Agriculture	1, 303	114
Forestry and fisheries	54	235
Coal mining	554	478
Crude petroleum and natural gas extraction	157	320
Mining and quarrying, except fuel	194	473
Construction	1, 371	181
Logging	361	1, 031
Sawmills, planing mills, and mill work	250	223
Railroads and railway express service	435	152
Trucking service and warehousing	520	382
Air transportation	53	331
Electric and gas utilities	223	217

[1] From Intermediate List (*1*).

NOTE: "n.e.c."—not elsewhere classified.

Industry

Figure 2 isolates four major industry groups in which the standardized mortality ratios for work accidents are high. In descending order these are "mining"; "transportation, communication, and other public utilities"; "construction"; and "agriculture, forestry, and fisheries." The industries listed in the Intermediate List (*1*) for which both the standardized mortality ratio and proportionate mortality ratio are high are shown in table 3. Two of the industries, "logging" and "sawmills, planing mills, and mill work," are in the major group, "manufacturing," for which the standardized mortality ratio as a whole is not high, while the risk of death from accidents in the remaining industries listed is reflected in the high standardized mortality ratios for their major groups.

Accidents Away From Work

The same procedure as that described for evaluating death rates for work accidents reported on death certificates for 1950 was

followed for evaluating the remainder of the accidental deaths—those specified on the death certificate as occurring away from work combined with those for which no information was given. The standardized mortality ratio and the proportionate mortality ratio were computed for each occupation and industry in the Intermediate List (*1*). Those for which both ratios were high are listed in table 4.

For nonoccupational accidents, consisting chiefly of motor vehicle and home accidents, considerably less variation in death rates would be expected among the major occupation or major industry groups, since these causes of death are not directly connected with work activity. The charts bear this out. However, there seems to be some correlation between the rates for deaths from accidents while as work and the rates for deaths from accidents away from work or "not stated." A possible explanation may be that the "not stated" group to some degree includes work accidents. Of the 15 occupations for which both the standardized mortality ratio and the proportionate mortality ratio for accidents away from work are high (table 4), 7 appear also in table 3. The seven industries shown in table 4 also appear in table 3. At a later date all accidents may be tabulated in further detail in order to produce a better understanding of the high standardized mortality ratios.

Table 4. Deaths from accidents away from work and unspecified, and standardized mortality ratios, men 20–64 years of age in selected occupations and industries,[1] United States, 1950

Occupation or industry	Number of deaths	Standardized mortality ratio
Occupation		
Farmers and farm laborers	4,554	126
Carpenters	701	110
Masons, tile setters, and stone cutters	160	134
Mechanics and repairmen, automobile	524	121
Structural metal workers	69	197
Mine operatives and laborers (n.e.c.)	839	209
Operatives and kindred workers (n.e.c.):		
Sawmills, planing mills, and miscellaneous wood products	174	157
Primary metal industries	199	120
Fishermen and oystermen	117	260
Lumbermen, raftsmen, and wood choppers	316	268
Other specified laborers	177	124
Laborers (n.e.c.):		
Furniture, saw and planing mills, miscellaneous wood products	343	301
Stone, clay, and glass products	114	224
Construction	961	193
Railroads and railway express service	471	248
Industry		
Agriculture	4,646	126
Forestry and fisheries	181	238
Crude petroleum and natural gas extraction	305	192
Construction	3,397	140
Logging	339	292
Sawmills, planing mills, and mill work	598	163
Railroads and railway express service	1,222	133

[1] From Intermediate List (*1*).

NOTE: "n.e.c."—not elsewhere classified.

Summary

Data are presented for mortality from accidents in 1950 among men 20–64 years of age, according to the occupation or industry reported on death certificates. Considerable difficulty exists in interpreting death rates based on usual occupation, requested on the death certificate, and the current occupation, enumerated on the census schedule, because of the frequent lack of correspondence between the two reports.

A method is suggested that permits the interpretation of the mortality data with a reasonable degree of confidence. Its application to accident mortality figures for 1950 shows that in that year death rates from accidents occurring at work were significantly high for men in certain of the manual occupations. For accidents occurring at places other than at work rates were high also for some of the manual occupations. About half of these occupations had been listed as having high rates for work accidents. It is unlikely that the high rates for these occupations are the results of errors in reporting occupation or industry. On the other hand, the criteria established for the selection of these occupations may result in omitting other high mortality groups because

reporting errors cannot be eliminated as a possible explanation of unusual rates.

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PUBLICATION ANNOUNCEMENTS

Address inquiries to publisher or sponsoring agency.

Check-Ups: Safeguarding Your Health. Public Affairs Pamphlet No. 314. By Michael H. K. Irwin, M.D., M.P.H. June 1961; 18 pages; 25 cents. Public Affairs Pamphlets, 22 East 38th St., New York 16.

Psychiatric Pilot Project. Publication No. 31. 1961; 25 pages. Institute for the Crippled and Disabled, Community Education Department, 400 First Ave., New York 10.

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Report of the Committee on the Control of Infectious Diseases. 1961; 132 pages; $1. American Academy of Pediatrics, 1801 Hinman Ave., Evanston, Ill.

Proceedings of the 15th Purdue Industrial Waste Conference. 1961; $3.50. Dean G. A. Hawkins, Engineering Administration Building, Purdue University, Lafayette, Ind.

Occupational Disease in California Attributed to Pesticides and Agricultural Chemicals, 1959. February 1961; 30 pages. California State Department of Public Health, 2151 Berkeley Way, Berkeley 4, Calif.

Salaries and Working Conditions of Social Welfare Manpower in 1960. 1961; 130 pages; $1.75. National Social Welfare Assembly, Inc., 345 East 46th St., New York 17.

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The Consistency of ACIR Accident-Injury Relationships in Four States. By B. J. Campbell. June 1961; 39 pages. Automotive Crash Injury Research of Cornell University, 316 East 61st St., New York 21.

Current Research and Development in Scientific Documentation, No. 8. NSF–61–29. National Science Foundation. May 1961; 193 pages; 65 cents. Superintendent of Documents, U.S. Government Printing Office, Washington 25, D.C.

Behavioral Approaches to Accident Research. 1961; 178 pages; $1.50. Association for the Aid of Crippled Children, 345 East 46th St., New York 17.

Health Care for the Aged in the State of Washington. HIF Perspectives No. a3. By Odin W. Anderson, Ph.D., and William T. Reich, Ph.D. 1961; 19 pages. Health Information Foundation, 420 Lexington Ave., New York 17.

Proceedings. Eighth Annual Meeting of National Citizens Committee for the World Health Organization, November 2–3, 1960. 49 pages; $1. National Citizens Committee for the World Health Organization, 1790 Broadway, New York 19.

SEC Technical Reports

A limited number of the following reports are available from the Sanitary Engineering Center, Public Health Service, Cincinnati, Ohio. Order by number.

Exhaust Contamination in Passenger Cars. A61–2. By Andrew H. Rose, Jr., Ralph C. Stahman, and Hever J. R. Stevenson. February 1961; 9 pages.

Publications. Section 2. Milk and food. F61–1. 1961; 13 pages.

Estuarine and Marine Pollution. Selected studies on biological, bacteriological, and physical aspects, with major emphasis on the United States literature. W61–4. By William Marcus Ingram and Thaddeus A. Wastler III. 1961; 30 pages.

Program Notes

New York City policemen have been ordered by the police commissioner to give out summonses to drivers of motor vehicles emitting unnecessary smoke. The department of air pollution has reported that the carbon monoxide content of the city air has risen from 1.4 to 3.5 parts per million during the past 5 years.

« »

Using funds accruing to the United States from the sale of agricultural surpluses (Public Law 480), translations of three Russian scientific publications on the nervous system have been issued: volume 1 of the pathophysiological series of the "Works of the Institute of Higher Nervous Activity of the Academy of Sciences of the U.S.S.R." (1955); A. N. Gordienko, "Control of Immunogenesis by the Nervous System" (1958); and R. E. Kayetskii, "The Neoplastic Process and the Nervous System" (1958). These translations have been distributed to medical libraries by the Office of Technical Services, Department of Commerce, for the National Science Foundation and the National Library of Medicine.

« »

Subscriptions to *Aging*, a monthly publication prepared by the Special Staff on Aging of the U.S. Department of Health, Education, and Welfare, have grown to more than 11,000. The Superintendent of Documents, Government Printing Office, Washington 25, D.C., sells subscriptions at $1.00 a year.

« »

Kentucky and Tennessee will each open a residential school for emotionally disturbed children in 1962. Each school will enroll 40 children, aged 6 to 12. The National Institute of Mental Health, Public Health Service, is aiding the establishment of the schools with a $1,962,000 grant. Part of this money will be allocated to the George Peabody College for Teachers in Nashville for training teachers, basic research in the problems of disturbed children, and a study of the effectiveness of the new schools.

The schools are intended for children whose mental illness is not severe enough to require hospitalization, but who cannot be cared for effectively as outpatients. They are not designed for mentally retarded children. The average stay will probably range from 1 to 4 months.

If the project is successful, Kentucky and Tennessee will eventually assume full support of the schools.

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The license for an atomic reactor at the University of Wyoming was suspended by the Atomic Energy Commission when an AEC inspector found the reactor in operation without a licensed person at the controls.

« »

Educational film strips with sound recorded in the Navajo language are being made by the Division of Indian Health, Public Health Service, in cooperation with the Navajo Tribal Community. The films, on subjects of nutrition, school health, development of water supplies, and trachoma control, will be employed in the tribal education program.

« »

"Lifetime Health Record," a book by Dr. David D. Rutstein, professor of preventive medicine at Harvard Medical School, encourages everyone to keep a lifetime personal health history, and tells how to do it. Spaces are provided for putting down information on family history, immunization, illnesses, X-rays, tests, and hospital admissions.

« »

A guide to the literature on laboratory animals has been compiled by Jules Cass and his co-workers at the University of Cincinnati. Literature on the procurement, maintenance, use, and intrinsic characteristics of the various species is listed and annotated.

The guide is Supplement 6 of a recent issue of *Federation Proceedings* titled "A Guide to Production, Care, and Use of Laboratory Animals." The *Proceedings* is published by the Federation of American Societies for Experimental Biology and Medicine.

The compilation of the bibliography was supported by a research grant from the National Institutes of Health.

« »

In a pilot project at the National Naval Medical Center, Bethesda, Md., nurses are learning about the medical application of nuclear energy and the nursing techniques and safety measures required in caring for patients receiving radioactive substances.

No graduate nursing program offers such training, although thousands of institutions in the country use radioisotopes for medical purposes. "Radioactive substances are drugs, and nurses are obligated by law to know the minimum and maximum dosages of drugs, their effects and the expected outcome," says Lt. Comdr. Lenore Simon, head of the Division of Nuclear Nursing at the Naval Medical Center.

« »

Of 400 male alcoholics in the New England area surveyed by Milton H. Maxwell of the Alcoholism Foundation, Alberta, Canada, 50 percent were able to keep their problem from showing while on the job for a year or more, 30 percent for 3 to 5 years, and the rest for 5 years or longer.

« »

A list of technical reports of the Robert A. Taft Sanitary Engineering Center, Public Health Service, has been issued. Requests for copies of the list may be addressed to the director of the center at Cincinnati 26, Ohio.

« »

A fountain-pen-shaped radiation monitor that "chirps" has been designed by Oak Ridge National Laboratory and is in production. The device is 6 inches long, weighs 3.5 ounces, and can be worn in the breastpocket by laboratory and industrial workers. At safe levels of radiation, the monitor chirps every 2 minutes. As radiation increases, the chirps blend to produce a tone of rising frequency.

Results of Diabetes Screening Activities, Fiscal Year 1959

GLEN W. McDONALD, M.D., QUENTIN R. REMEIN, and EDWARD J. DURDICK

IN THE FISCAL YEAR ending June 30, 1959, 19 States, 2 Territories, and the District of Columbia reported results of diabetes screening activities to the Public Health Service. A total of 176,893 persons were reported tested in programs throughout the United States with an additional 19,191 screened in the Territories. From approximately 7,000 persons who screened positive, more than 4,000 were referred to their physicians for diagnostic evaluation on the basis of abnormal screening or retest findings. Approximately 1,100 cases of diabetes were discovered among persons who were not previously aware that they had diabetes, and 706 cases previously known to their physicians were identified and the patients were referred back to their physicians for care.

The total of persons tested probably does not include all who were screened since frequently the screening done during National Diabetes Week in November is on such an informal basis that neither the number of tests nor the results are known. Also being limited to community programs, the total does not include screening done in doctors' offices, hospitals, or private clinics. While information about testing programs is diligently sought through the Public Health Service regional offices, State health departments, publications, and other sources, undoubtedly some screening programs may have been missed. Except for National Diabetes Week activities, it is believed that the volume of screening not reported is relatively small.

Much of the testing during the year was done in the northeastern United States (table 1 and map). Some screening was also conducted in the Rocky Mountain and western plains areas, where a higher rate per population was achieved. The reported screening rate per 1,000 population ranged from 0.1 to 46.0 with an average of about 2 per 1,000 population tested. Only five reporting States tested more than 5 per 1,000 of the population, indicating that only a small segment of the population was reached.

From the distribution of persons tested (table 2), it may be generalized that practically all were in programs testing blood specimens. Studies have shown that blood sugar screening tests indicate more diabetics than do urine tests when they are compared at levels where each test separates out the same proportion of nondiabetics (*1*). Of the total persons reported tested only about 3,000 (2.3 percent) were in programs which used any urine sceening at all, and only a minute fraction (0.3 percent) were tested solely for urine sugar. Table 3 shows that almost 90,000 persons were tested in programs conducted for the general population; testing directed at employee groups accounted for the next largest number, 25,000 persons. The age data indicate that the programs have not concentrated on the older age groups in which the probability of having diabetes is higher. Since screening for diabetes is frequently coupled with other types of screening,

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Table 1. Diabetes screening activity reported to Public Health Service during fiscal year 1959, by geographic area

Area	Persons tested			Screened positive	Positive after screening and retesting	Referred to physician	Number of cases found	
	All programs		Followup programs				Known	New
	Total	Rate per 1,000 population [1]						
States	176,893	2.2	154,544	7,065	[2] 4,440	4,064	706	1,105
Arizona	14,333	11.8	14,333	511	235	235	64	69
Colorado	14,588	8.8	14,588	178	178	178	45	27
Connecticut	505	.2	505	13	13	13	7	2
District of Columbia	37,687	46.0	37,687	1,898	841	643	127	376
Florida	615	.1	615	19	15	13	6	4
Hawaii	18,641	31.1	18,641	1,347	[2] 288	288	116	172
Iowa	3,267	1.2	2,267	123	71	60	0	33
Kansas	11,342	5.4	9,692	257	257	257	77	46
Kentucky	4,208	1.4	4,208	136	105	77	9	13
Maine	2,736	2.9	2,736	28	28	28	4	5
Michigan	14,275	1.8	14,275	179	179	179	24	72
Nevada	1,090	4.0	1,090	32	32	32	0	1
New York	17,964	1.1	2,143	670	670	670	29	28
North Carolina	2,382	.5	2,025	201	165	99	22	29
Ohio	12,244	1.3	12,244	574	464	393	39	71
Oklahoma	1,682	.8	1,288	41	41	41	0	8
Pennsylvania	5,272	.5	5,272	218	218	218	25	41
Tennessee [3]	2,189	.6	2,189	199	199	199	39	59
Virginia	8,746	2.3	8,746	306	306	306	73	49
West Virginia	3,127	1.6	0	135	135	135	----	----
Territories	19,191	([4])	19,191	859	719	464	124	173
Puerto Rico	9,313	([4])	9,313	712	582	375	120	94
Virgin Islands	9,878	([4])	9,878	147	137	89	4	79

[1] Estimated civilian population, Dec. 27, 1959, U.S. Bureau of the Census, Current Population Reports, P–25, No. 210.
[2] Number screened positive used when retesting program did not specify retest results.
[3] Health card screenees only.
[4] Not available.

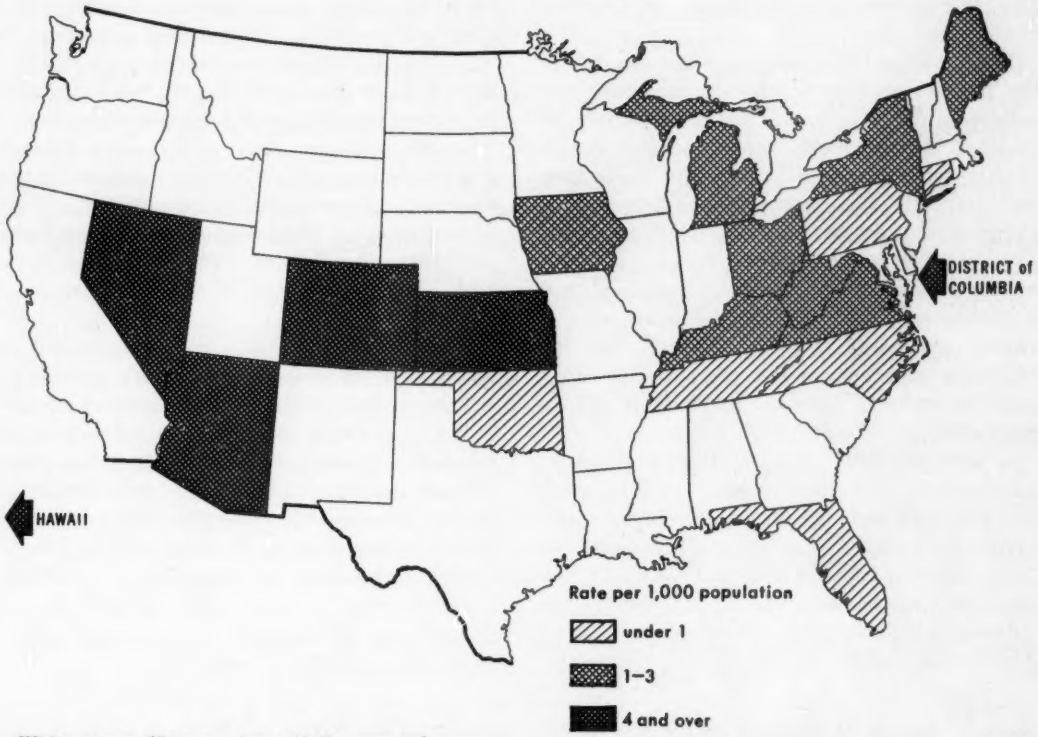
it is possible that the selection of age groups was influenced by factors not associated with diabetes, as for example in syphilis detection and in college or pre-employment health examinations.

More than half the initial blood sugar tests were performed on blood specimens screened at levels up to 130 mg./100 ml. On the assumption that the severity of diabetes is directly correlated with the level of blood sugar, a low screening level will detect mild or early diabetes in addition to the severe cases, but it will also result in more false positives. False positives may be separated out by retesting. Half the persons tested in the country, according to the reports, were in programs where retesting was done on all or on certain categories of participants with positive tests on initial screening before referrals were made to private physicians for diagnosis and treatment.

Retesting

Retesting is the reexamination of positive screenees under more carefully controlled circumstances, that is, at a set time after a high carbohydrate meal or after glucose ingestion. This reexamination is a confirmatory test to refine the number of initial positives to persons more likely to have diabetes. This method avoids swamping physicians with large numbers of persons who do not have diabetes, thus reducing costly and time-consuming inconven-

Diabetes cases reported to the Public Health Service as a result of screening activities, fiscal year 1959



White areas—No screening activity reported.

ience to both physician and screenee, and contributes greatly to the maintenance of physician interest and cooperation. The benefits of retesting can be seen in table 4, which shows that a little more than one-third of the persons with initial positive results are referred to physicians. A second benefit is that among these fewer referrals there is a higher concentration of diabetics. Table 4 also shows that the proportion of diabetes cases found among retested referrals is more than twice that found in the referrals from an initial screening test only. Some caution is in order since unknown factors, such as characteristics of the population screened and pretest eating requirements, may be operating to affect the results. Generally, the data support the value of including retest procedures before patients are referred to a physician. Program directors should consider the advantages of retesting even though a few cases may be missed. One should weigh the cost of followup and diagnosis of all positive screenees against the cost of retesting this group and the followup or diagnosis of approximately half of them.

Followup

Screening programs use followup to make sure that suspects pursue the course required to establish or rule out diabetes or to assure their return to treatment, as well as to obtain the cooperation of physicians in reporting dispositions of referrals. In screening programs doing followup there is evidence that diagnostic procedures had been completed on 78 percent of the 2,991 suspects referred to their physicians for diagnosis. A certain amount of time must be allowed for physicians to complete diagnostic procedures and report the results. The Public Health Service recommends that up to 90 days be allowed for making diagnoses and reporting dispositions of cases. Because of this

need for time to complete diagnoses, there undoubtedly will be later determinations on many dispositions reported as incomplete at the time of the cutoff date.

Nationally, a little more than one-quarter of the positive screenees referred to physicians between July 1, 1958, and June 30, 1959, were found to be nondiabetic, but this number varied greatly from program to program depending on diagnostic standards, type of population, age groups, the test used, and extent of retesting before referral to a physician. Positive screenees currently diagnosed nondiabetic are a profitable group for future casefinding. A recent community study has shown that the incidence rate among persons once screening positive is 8 to 10 times the rate among persons previously screening negative (*2*).

Almost one-fifth of the followup program participants who were referred to physicians for diagnosis were reported to have previously known diabetes. Unfortunately this figure has little meaning epidemiologically since it depends in large measure on program policies for processing known cases. These policies varied greatly among the programs. In some instances people were advised in publicity material not to present themselves for screening if they had already been told by a physician that they had diabetes. There were programs in which people were questioned at screening and turned away if they said they were diabetic. In other programs no questions were asked. There is, however, some advantage to including previously known diabetics in a screening program. These diabetics are referred to their physicians, and thus, contact between patients and their physicians is strengthened, and those who had lapsed from care are returned to medical supervision.

Almost a third of the persons referred to physicians for diagnosis represent previously unknown cases of diabetes. The overall yield is 6.9 new cases reported per 1,000 persons screened. As can be seen from the tables there is much variation in the yields for various categories. Because the various population groups shown were served by different screening techniques combined with different followup methods, a higher yield drawn from one group does not necessarily indicate a higher diabetes prevalence existing in that group.

Table 2. Results of diabetes casefinding activity reported to the Public Health Service,[1] fiscal year 1959

Screening method	Persons tested in followup programs		Results of followup							
			Total completed		No diabetes		Known cases		New cases	
	Total	Referred to physician	Number	Percent of referred	Number	Percent of followup	Number	Percent of cases found	Number	Yield per 1,000 tested
All methods	135,903	2,991	2,344	78.4	821	35.0	590	38.7	933	6.9
Single test	66,854	1,588	1,264	79.6	600	47.5	325	48.9	339	5.1
Retest	69,049	1,403	1,080	77.0	221	20.5	265	30.8	594	8.6
Blood, 130 mg./100 ml. or less	75,923	1,631	1,231	75.5	333	27.1	309	34.4	589	7 8
Single test	13,871	500	390	78.0	204	52.3	89	47.8	97	7.0
Retest	62,052	1,131	841	74.4	129	15.3	220	30.9	492	7.9
Blood, above 130 mg./100 ml	56,882	1,086	873	80.4	382	43.8	226	46.1	265	4.7
Single test	52,074	1,013	812	80.2	370	45.6	220	49.8	222	4.3
Retest	4,808	73	61	83.6	12	19.7	6	12.2	43	8.9
Blood and urine[2]	2,713	260	226	86.9	93	41.2	55	41.4	78	28.8
Single test	524	61	48	78.7	13	27.1	16	45.7	19	36.3
Retest	2,189	199	178	89.4	80	44.9	39	39.8	59	27.0
Urine alone, single test	385	14	14	100.0	13	92.9	0	-------	1	2.6

[1] For comparability, Hawaii excluded since followup data not sufficiently reported.
[2] Data from special research projects not indicative of usual programs.

The yield of previously unknown cases of diabetes was about a third greater in programs using screening levels of 130 mg./100 ml. or below than it was in programs which had higher screening levels, for example, 160 and 180 mg./100 ml. The yield was 7.8 cases per 1,000 screenees for programs which screened at levels up to 130 mg./100 ml. and 4.7 per 1,000 for program screening at levels above 130 mg./100 ml. Here again differences in techniques are involved, but recent studies support this finding (*3*).

Age

By age there are great differences in yield of diabetes cases. Persons 45 years of age and over produced yield rates five to six times as great as persons in the age group 20–44 years. Almost three-fifths of the screenees for whom age was reported were in this younger age group. Program efficiency, in terms of yield of cases, could be greatly increased by shifting screening effort from the low-yield younger age groups to the high-yield older age groups.

The progressive rise of rates with age was consistently noted in the individual programs reporting, as was the rate drop in the age groups over 75 years. This latter condition may be partly explained by selective forces of mortality operating to remove diabetics from this age bracket. It appears, from the programs for which age data are available, that perhaps programs cognizant of the ages of persons tested do better than other programs, since the overall yield in the former is almost twice as high as the yield in the latter.

Discussion and Summary

A thorough health maintenance examination once a year is considered an ideal way for a person to safeguard his health, particularly after the age of 40. A proper examination of this type includes a medical history, physical examination, and laboratory tests and procedures.

Table 3. Population characteristics and age of screenees in diabetes casefinding activities reported to the Public Health Service, fiscal year 1959

Population group and age (years)	Persons tested in followup programs		Results of followup							
			Total completed		No diabetes		Known cases		New cases	
	Total	Referred to physician	Number	Percent of referred	Number	Percent of followup	Number	Percent of cases found	Number	Yield per 1,000 tested
Total population	135, 903	2, 991	2, 344	78. 4	821	35. 0	590	38. 7	933	6. 9
General	89, 850	1, 904	1, 513	79. 5	457	30. 2	388	36. 7	668	7. 4
Employees	25, 270	260	230	88. 5	115	50. 0	51	44. 3	64	9. 7
Low income and welfare	8, 486	209	121	57. 9	40	33. 1	47	58. 0	34	4. 0
Clinic patients	7, 891	112	94	83. 9	19	20. 2	23	30. 7	52	6. 6
Inpatients	6, 886	160	133	83. 1	48	36. 1	40	47. 1	45	6. 5
Suspects	11, 809	255	196	76. 9	103	52. 6	36	38. 7	57	4. 8
Detention	3, 354	44	22	50. 0	10	45. 5	5	41. 7	7	2. 1
Students	385	14	14	100. 0	13	92. 9	0	-------	1	2. 6
Other	613	33	21	63. 6	16	76. 2	0	-------	5	8. 2
All ages [1]	49, 958	1, 083	882	81. 4	160	18. 1	224	31. 0	498	10. 0
Under 20	4, 086	8	5	62. 5	0	-------	1	20. 0	4	1. 0
20–44	29, 380	321	245	76. 3	57	23. 3	51	27. 1	137	4. 7
45–64	13, 103	568	484	85. 2	73	15. 1	124	30. 2	287	21. 9
65–74	2, 081	132	108	81. 8	16	14. 8	39	42. 4	53	25. 5
75–84	575	40	31	77. 5	8	25. 8	9	39. 1	14	24. 3
85 and over	96	3	3	100. 0	3	100. 0	0	-------	0	-------
Unknown	637	11	6	54. 5	3	50. 0	0	-------	3	4. 7

[1] Includes only programs reporting by age.

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Performance of laboratory tests for the entire population is impractical because the number of physicians, their necessary equipment, and the amount of funds needed by individuals and communities would be enormous. In view of the number of patients with obvious medical problems, busy physicians have difficulty finding time to make repeated routine examinations of presumably healthy persons. One of the most useful devices for conserving physician services is the public health screening program —using simple, inexpensive tests that can be given in a relatively short time to a large number of apparently well persons to sort out those who may have a disease from those who probably do not. The data in this report reveal that people, probably conscientious in safeguarding their health, are taking advantage of diabetes screening opportunities. However, the figures also show that for almost 50 percent of all persons with positive test results, no information was reported about their diagnostic status. In the 19 States reporting diabetes screening activities, more than 8 percent of the 4,440 persons with positive test results were not referred to a physician for diagnosis; for about 40 percent no diagnostic reports were received.

Diabetes screening programs, no matter how well designed and operated, are of little value as a community service unless all individuals screened as probably having the disease are followed for confirmation of whether or not they have diabetes. In turn, a diagnosis of diabetes is meaningless unless it is followed by medical care. Without followup, screening programs have not fulfilled their implied obligation to help maintain the health of participants who come to the screening line believing that they will receive a health service.

Screening is offered, by definition, to persons who are presumably free of the disease being screened. If an individual has a positive screening test, he has a right to know at the earliest possible time whether he can be reassured about his health or whether he is fortunate that diabetes has been diagnosed and treatment will begin promptly. When screening activities process persons who already have the disease, an additional contribution can be made by returning lapsed cases to treatment or by providing an opportuntiy for the physician to check that the benefits of therapy are being maintained.

From an administrative standpoint followup results are vital to the evaluation of a program. The yield in new cases is an important factor in measuring the success of a program, and a case is identified only when it is diagnosed by a physician. Data on yield of new cases can serve adequately to compare types of programs when these data are qualified according to variables such as screening test results and blood sugar level, age, sex, and socioeconomic group.

Reporting only on persons for whom a diagnosis has been made does not complete the followup process. Enumeration of persons not yet diagnosed by the physician to whom they were referred is necessary to evaluate followup procedures. Dawdling suspects and delayed reporting should be expedited by letter or a visit by a member of the program. Tabulations by the various causes of incomplete dispositions can well serve to indicate where breakdowns may have occurred in the followup procedure. A well-functioning followup system will reveal

Table. 4. New cases of diabetes found in selected casefinding programs, before and after retesting

Initial blood sugar level	Total cases found in initial screening	Referred for diagnosis		New cases found		
		Number	Percent	Number	Percent of—	
					Initial cases	Referred cases
130 mg./100 ml. or less:						
Not retested	501	500	99. 8	97	19. 4	19. 4
Retested	2, 848	1, 131	39. 7	492	17. 3	43. 5
160 mg./100 ml.:						
Not retested	847	834	98. 5	186	22. 0	22. 3
Retested	207	73	35. 3	43	20. 8	58. 9

the extent to which the diabetes screening program was successful in assuring that every person with a suspicion of diabetes was diagnosed and, if necessary, brought under treatment.

Reports of diabetes screening during fiscal year 1959 indicate that in each 1,000 persons tested, 40 persons had positive screening tests. Through retesting or loss during the referral process this number dropped to 23 who were referred to their physicians. Definitive diagnostic procedures were carried out for 17 persons. Approximately 10 persons per 1,000 in the screened population were diagnosed as having diabetes, of which 7 were new cases.

Programs being planned should consider these results as minimal. Detecting new cases of diabetes in nearly 0.7 percent of the population when compared with estimates of more than 0.8 percent in the literature (*4*) indicates a need for improvement in trying to reach all those people in the United States who have unrecognized diabetes. Programs should logically be more effective if they are directed toward known high diabetes prevalence groups such as persons over 40, relatives of diabetics, the obese, parents of large babies (over 9 pounds), and medical patients. In addition, programs should emphasize blood sugar testing, particularly of specimens obtained at set postprandial periods, as contrasted with specimens obtained at random times. Program planners should also consider the value of retesting, should use standardized diagnostic procedures, and should concentrate more effort on followup procedures (*5*). Optimal utilization of diabetes detection programs should produce yields greater than the national prevalence rate.

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Seat Belts and Blowby Devices

The General Services Administration of the Federal Government now requires all motor vehicles purchased by GSA to have seat-belt anchors and positive crankcase ventilation systems to reduce "blowby" emissions. GSA currently buys about 7,000 motor vehicles yearly to serve the various Federal agencies.

The "blowby" devices reduce the amount of gases, mostly hydrocarbons from unburned gasoline, which blow by the piston rings and into the atmosphere, contributing to air pollution. According to Dr. Luther L. Terry, Surgeon General of the Public Health Service, the devices required by GSA "are highly desirable, reducing total automotive emissions of hydrocarbons by about 25 percent at a very nominal cost." "As for seat belts," Dr. Terry said, "the best available statistics indicate that about 5,000 lives now being lost annually in automobile accidents could be saved through their universal use."

EXPERIENCE WITH VDRL FLOCCULATION ANTIGEN IN THE KOLMER COMPLEMENT FIXATION TEST

Albert Dickman, Ph.D.

IN RECENT years interest has been concentrated on treponemal antigens and little attention has apparently been given to improvement of the currently available nontreponemal antigens. This is unfortunate, since an easily available lipoidal antigen with improved specificity would be of extreme value in the laboratory.

In the United States, with its premarital and prenatal laws, millions of serologic tests for syphilis are performed on presumably healthy individuals. All too frequently, particularly with cardiolipin antigens commercially available, reactive laboratory findings are obtained which are not supported by clinical findings.

Various estimates of biologic false positive reactions with routine procedures have been advanced by various authors. Variation in these figures is wide. They, of course, are influenced by the type of population group evaluated, the serologic procedures and type of antigen employed, and the definition of positivity used.

Deservedly or not, the current criterion of the value of a serologic test for syphilis is its sensitivity and specificity in comparison with the sensitivity and specificity of the *Treponema pallidum* immobilization (TPI) test of Nelson and Mayer.

Using the TPI test as a reference, rather high false positive figures have been found with standard lipoidal antigens.

MacPherson, Ledbetter, and Martens (*1*) reported results of 21 to 40 percent of routine reactive tests as biologic false positives, and a number of other authors, including Moore and Lutz (*2*), reported 40 percent false positives,

In a comparative study of 572 "problem serums" which were reactive with nontreponemal tests, Wilkinson (*3*) found that the Kahn test gave 17 percent nonspecific reactions, the Wassermann test with lipoidal antigen 13 percent, and the Wassermann test with cardiolipin antigen 23 percent. In 244 patients found to be seropositive on routine testing during pregnancy, blood tests of 27.5 percent gave presumed nonspecific reactions.

In our own laboratory, of 796 reactive VDRL slide tests, 435, or 54.6 percent, were assumed to be biologic false positives, with the TPI test used as the reference test. Of 724 reactive cardiolipin Kolmer tests, 385, or 53.2 percent, were in the same category. These figures were obtained on specimens submitted to us for TPI tests, and these cases can consequently be placed in the "problem" category.

VDRL Flocculation Antigen as CF Antigen

There would be considerable advantage in being able to use the same antigen for both flocculation and complement fixation tests. In the Dickman Laboratories the VDRL antigen with its current composition seems to fall into this category. Our preliminary studies indicate that the VDRL antigen might profitably be evaluated in a future national survey such as the Serology Evaluation Research Assembly study recently completed by the Public Health Service. There might be further advantage in determining whether the cardiolipin-lecithin-cholesterol ratio of other commonly used antigens is the optimum when used with the TPI test as the reference test.

For many years we have performed a considerable number of serologic tests for syphilis, and since we are located in Pennsylvania, a State whose premarital law requires both a flocculation and a complement fixation test on each specimen of blood, we have routinely carried out both procedures. Most of the speci-

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mens examined in our laboratory are submitted for premarital tests, and we can assume that the majority of them come from a young, generally healthy group of individuals of satisfactory social and economic background. In a series of 64,206 premarital blood tests employing lipoidal antigens, 1.08 percent were reported as reactive in both flocculation and complement fixation techniques.

Having run both flocculation and complement fixation tests on each specimen of blood over a period of more than 20 years, and having at various times during this period employed the VDRL, Eagle flocculation, Hinton, Mazzini, Eagle complement fixation, and Kolmer complement fixation tests with crude lipoidal and cardiolipin antigens, we have been able to observe the behavior of the various tests on groups of specimens predominantly from presumably healthy nonsyphilitic individuals. Furthermore, we have had ample opportunity to evaluate the various techniques on serums of known reactivity in the monthly State department of health evaluations.

Since cardiolipin antigens became available we have gradually restricted ourselves to the use of the VDRL slide test and the Kolmer complement fixation test using cardiolipin antigens. In the monthly State evaluations we have consistently obtained excellent agreement between results of the two techniques on the pooled serums submitted, but in the higher dilutions of the positive test serums we have found the Kolmer test consistently the more strongly reactive.

Over the years, among the blood specimens submitted to us for diagnostic tests on treated or suspected syphilitic persons, the agreement in findings of the Kolmer and VDRL slide tests has been generally close. Since our change to cardiolipin antigens, however, and particularly since employment of commercially available antigens, we have been considerably concerned with what appears to us to be an inordinate number of weak reactions with the Kolmer complement fixation technique, coupled with nonreactive VDRL findings among our premarital and prenatal specimens. We have investigated every possible factor affecting performance of the tests and have gained the impression from questioning other laboratories that they are having similar experiences with commercial antigens employed at the recommended dilutions.

In 1948, Kolmer stated that six different antigens employing various ratios of cardiolipin, purified lecithin, and cholesterol might be employed in the Kolmer tests in doses of 0.5 ml. of a 1:150 dilution. The acceptable formulas are given in table 1. Kolmer also stated that in general an antigen prepared with 0.03 percent cardiolipin, 0.05 percent lecithin, and 0.6 percent cholesterol was preferred as a mixture having maximum sensitivity consistent with specificity in tests with serums and spinal fluids (*4*).

The currently available Kolmer antigen contains 0.03 percent cardiolipin, 0.05 percent lecithin, and 0.3 percent cholesterol. The optimum dose recommended has been in every case 0.5 ml. of a 1:150 dilution. In this study, we have in addition employed as an antigen for the Kolmer test one placed on the market as a VDRL flocculation antigen. It contains, in addition to lecithin, 0.05 percent cardiolipin and 0.9 percent cholesterol.

Although every commercial package of Kolmer antigen recommends a dilution of 1:150, a number of antigen titrations on lots from two major producers (Difco and Sylvana) gave a titer of 1:320 when carried out by the recommended procedure. The 1:320 dilution was found to be optimum for the VDRL flocculation antigen when it was used as a complement fixation antigen. In various sets of State evaluations of serums there seemed to be no significant loss in sensitivity when the 1:320 dilution of Kolmer antigens was used with either 0.9 percent or 0.3 percent cholesterol. There has been no evidence of increased anticomplemen-

Table 1. Formulas for antigens acceptable for use in Kolmer tests [1]

Antigen No.	Cardiolipin (percent)	Purified lecithin (percent)	Cholesterol (percent)
1	0.03	0.05	0.3
2	.03	.05	.6
3	.03	.05	.9
4	.06	.05	.6
5	.06	.05	.9
6	.175	.0875	.3

[1] Kolmer, J. A., and Lynch, E. R. (*4*).

tary activity in any of the dilutions employed. On the other hand, there does seem to be a decided difference in specificity of the two antigens when used on routine specimens submitted to the laboratory.

In our laboratory we have found that an antigen containing 0.03 percent cardiolipin, approximately 0.21 percent lecithin, and 0.9 percent cholesterol—the composition of standard VDRL flocculation antigen—when used in a test dose of 0.5 ml. of a 1:320 dilution in the standard Kolmer procedure, has a high degree of sensitivity when compared with various approved techniques, including the standard Kolmer test in State evaluations on positive serums of known activity. Compared with the standard Kolmer test, however, the complement fixation test with VDRL antigen gives fewer confusing weak reactions in presumably negative serums.

Weak reactions cannot be taken lightly, yet in those cases which we have been able to check with the TPI test there is an indication that the weakly reactive standard Kolmer reactions in the presence of nonreactive VDRL slide tests are very often nonspecific.

Table 2 shows that, in comparison with other standard procedures, use of an antigen having the composition of VDRL flocculation antigen in the Kolmer test, in a test dose of 0.5 ml. of a

Table 2. Comparison of reaction of VDRL flocculation antigen used as a complement fixation antigen in a test dose [1] with reference findings in a routine State evaluation

Test	Positive dilutions												Negative serums							
	1:4	1:4	1:8	1:8	1:16	1:16	1:16	1:16	1:24	1:24	1:24	1:24	N	N	N	N	N	N	N	N
VDRL slide [2]	R	R	R	R	R	R	R	R	R	R	R	R	N	N	N	N	N	N	N	N
VDRL tube [2]	R	R	R	R	R	R	R	R	R	R	R	R	N	N	N	N	N	N	N	N
Kline standard [2]	4	4	4	4	2	2	2	2	1	1	1	1	N	N	N	N	N	N	N	N
Kahn standard [2]	4	4	3	2	1	1	1	1	1	±	1	±	N	N	N	N	N	N	N	N
Mazzini cardiolipin [2]	4	4	4	4	2	2	2	2	N	N	N	N	N	N	N	N	N	N	N	N
Hinton flocculation [2]	R	R	R	R	R	R	R	R	R	R	R	R	N	N	N	N	N	N	N	N
Kolmer cardiolipin [2]	4	4	4	4	3	3	4	3	1	2	1	1	N	N	N	N	N	N	N	N
Kolmer lipoidal [2]	4	4	2	1	±	N	±	N	N	N	N	N	N	N	N	N	N	N	N	N
Kolmer using VDRL flocculation antigen [1 3]	4	4	4	4	4	4	4	4	1	2	1	1	N	N	N	N	N	N	N	N

[1] 0.5 ml. of a 1:320 dilution.
[2] Reference laboratory.
[3] Dickman Laboratories, Philadelphia, Pa.

NOTE: R—reactive; N—negative.

Table 3. Results of testing 86 blood specimens with the Kolmer standard, VDRL slide, Kolmer with VDRL antigen, and TPI tests

Number of tests	Kolmer standard test	VDRL slide test	Kolmer test using VDRL antigen (1:320)	TPI test
1	++++	NR	±	Negative.
1	++++	NR	+	Positive.
1	++++	NR	++	Do.
1	++++	NR	+++	Do.
1	++++	NR	++++	Do.
3	++++	NR	NR	Negative.
24	++++	NR	NR	Do.
11	+++	NR	NR	Do.
14	++	NR	NR	Do.
22	+	NR	NR	Do.
7	±	NR	NR	Do.

NR—nonreactive.

1:320 dilution, results in a very satisfactory performance. In our laboratory, in a series of 5,215 predominantly premarital blood specimens which were tested with the VDRL slide test and the Kolmer technique with the VDRL flocculation antigen, 51, or 0.98 percent, were reported reactive by both techniques and 35, or 0.67 percent, were reported as doubtful. The doubtful group consisted of specimens in which there was disagreement between the findings of the two tests. In 5,129 of the 5,215 specimens, both tests were nonreactive.

We have further checked at random some specimens submitted to us primarily for premarital or prenatal tests in which there were reactive findings in the standard Kolmer test employing standard antigen in a dilution of 1:150 and nonreactive findings in the VDRL slide test. Complement fixation tests, employing the Kolmer technique with a VDRL flocculation antigen containing 0.03 percent cardiolipin and 0.9 percent cholesterol in a dilution of 1:320, and a TPI test were performed.

The results of testing a series of 86 specimens, of which 68 were submitted for premarital tests, are given in table 3. The four tests in this series which were positive by the TPI test were all reactive to the Kolmer test using VDRL flocculation antigen. In the presence of nonreactive VDRL flocculation tests 82 of the 86 standard Kolmer tests gave presumably biologic false positive reactions.

Most of these blood specimens came from a group in which a low incidence of reactivity is to be anticipated. The significance of a questionable reaction probably varies considerably with the social and economic group from which the individual comes. A reactive finding is less likely to be a biologic false positive in an individual from a group in which the syphilis rate is high than in an individual from a group in which the incidence of syphilis is extremely low.

Kolmer Test in Problem Cases

In our experience, there seems to be considerable evidence of the advantage of using the VDRL flocculation antigen as a complement fixation antigen in analyzing routine specimens.

On 827 of the more than 1,100 "problem specimens" sent to us for TPI determinations, we were able to perform, in addition to the TPI test, both the standard Kolmer and the Kolmer complement fixation technique employing VDRL flocculation antigen in a 1:320 dilution. The results are shown in table 4.

Table 4. Comparison of results of TPI tests on 827 "problem specimens" with results of the Kolmer test with VDRL antigen and the standard Kolmer test

TPI test	Kolmer test with VDRL antigen [1]		Standard Kolmer test	
	Reactive	Nonreactive	Reactive	Nonreactive
Negative	190	322	331	181
Positive	252	63	285	30

[1] 0.5 ml. of 1:320 dilution.

In this group of 616 tests reactive with the standard Kolmer test 331, or 53.7 percent of the reactions may be presumed to be nonspecific. With the use of VDRL antigen as a complement fixation antigen in a Kolmer technique, of the 442 reactive specimens, 190, or 43.0 percent, may be considered nonspecific. Of the 63 TPI-positive specimens giving negative reactions with the experimental VDRL antigen, 28 were nonreactive and 35 were reactive in the VDRL slide test.

Summary

Of 796 reactive "problem specimens" of blood submitted to the Dickman Laboratories for *Treponema pallidum* immobilization tests, 54.6 percent were probably biologic false positive by the VDRL slide flocculation test and 53.2 percent by the standard Kolmer complement fixation test.

In "problem cases" there seems to be no relationship between the degree of reactivity in the standard lipoidal tests and TPI positivity. In a considerable number of routine laboratory specimens, however, weak Kolmer reactions in the presence of negative VDRL slide tests are nonspecific.

The VDRL flocculation antigen in a test dose of 0.5 ml. of a 1:320 dilution would appear to offer significant advantages as a complement fixation antigen in the Kolmer technique. In

general practice VDRL flocculation antigen has a high degree of sensitivity and specificity and, as confirmed by TPI tests, gives fewer questionable weak reactions in the average presumably negative specimens submitted to the laboratory. In problem cases there are fewer nonspecific reactions with the VDRL antigen than with the standard Kolmer antigen and, when run in conjunction with a VDRL slide test, the VDRL antigen should prove to be a desirable substitute for the current standard Kolmer antigen in the laboratory.

It would be profitable to study further experimental compositions and modifications of our currently employed lipoidal antigens in future serologic studies.

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VD Educational Materials

Educational materials pertaining to venereal disease and teenagers are available for meetings and discussion groups, free of charge, from the Venereal Disease Branch of the Communicable Disease Center, Public Health Service. The branch also performs special services, such as providing current data, studies, and reprints. Some of the materials offered are:

Films. "The Innocent Party" shows how a teenage boy contracts venereal disease from a pickup and its consequences. "The Invader" traces man's efforts since the 15th century to cope with syphilis.

Exhibit. "Who has VD?" demonstrates an actual outbreak of syphilis and gonorrhea as it occurred in a small community.

Literature. "Strictly for Teenagers" provides factual answers about venereal disease to teenage questions. "About Syphilis and Gonorrhea" explains briefly the cause, spread, and cure of these diseases. "Public Pressure Hinders Work of VD Eradication" challenges responsible individuals to remember their community obligations and prods community leaders to aid in public enlightenment. "VD in Children and Youth" describes venereal disease and its control problems, particularly as related to teenagers. This 32-page booklet contains advanced information for discussion leaders and writers.

For further information or to be placed on a mailing list for announcements or samples of new materials write to William J. Brown, M.D., Chief, Venereal Disease Branch, Communicable Disease Center, Public Health Service, Atlanta 22, Ga.

Public Health in Ohio

The effect of culture and society upon public health and the pattern of increased pace and rapid growth of activities in public health work are two related subjects covered at the May 19, 1960, meeting of the Ohio Public Health Association. We present two papers on these topics, one showing where and how culture and society and public health meet; the other pointing up today's challenges to public health and how they may be faced.

Growth Pattern in Health Work

brief

The increased pace and rapid growth of public health activities in Ohio follow a pattern which can be divided into three categories: a new and vigorous attack on some old problems which have long been neglected; an attack on some new aspects of old problems; and an attack on totally new problems.

In the first category is the new public health program for alcoholism. There are an estimated 200,000 alcoholics in Ohio today who, together with their families, may represent as high as 10 percent of the total population. Alcoholics can be helped. Previous programs for the most part were geared to helping those in the final stages of their illness after personal disintegration and family disruption had become critical. The goal of our present program encompasses the preventive aspects of reaching and helping them in the early stages.

Expansion of our chronic disease and geriatrics program also comes under this category. We have been concentrating on the maladies of the younger years. Ironically, as we become more successful in these endeavors our problem of the aged increases. There is need to step up our efforts against the chronic diseases, and we should continue them in the hope that the result will compare favorably with our success in the field of communicable diseases.

In neglected older problems toward which new programs are geared might be included the licensing and inspection of nursing homes, recently transferred to the Ohio State Department of Health from other departments, and the inspection and licensing of general hospitals.

In the second category, new aspects of old problems, would fall, for example, "hot strains"

Based on a paper by Ralph E. Dwork, M.D., M.P.H., director of the Ohio Department of Health.

of staphylococcal infection. Because of the impressive early effects of the antibiotics on pathogenic bacteria, we let down our guard and became too complacent. Now realizing some limitations of these medications, we are gaining new respect for established antiseptic techniques.

There are in Ohio sources of some as yet unclassified mycobacteria which cause a tuberculosis-like disease and are resistant to the chemotherapy that is effective with the tubercle bacillus. Though not serious enough for alarm, the infection is of sufficient importance for us to be on the alert. We are concentrating on improved laboratory and diagnostic techniques which will permit better evaluation of the situation and assure preventive steps against the disease.

The old question of food sanitation appears in a new guise in food vending machines. The State's new program for their licensing and inspection uses much the same methods as formerly except that we now have to probe into the machines rather than under counters and into backrooms.

Many of the problems in the third category are man made, nonexistent or unrecognized a few years ago: air pollution, radiation, and the explosive spreading of urban populations into small units scattered across the countryside.

The pouring of all kinds of material into the atmosphere is making a chemical monstrosity of the air we breathe. Part of our attack against this hazard is an elaborate new laboratory in the State health department which will be available to assist local areas in air pollution surveys. State technicians will help train local personnel, thereby enabling them to continue the observations. Regulation of air pollution is primarily a local activity in which the State can assist.

Supervision of the diagnostic, therapeutic, and industrial use of radium and X-ray is relatively new in the field of public health. It is estimated there are 10,000 medical and dental users of X-rays in Ohio, at least 250 industrial and medical users of radioisotopes, and approximately 200 industrial users of X-ray and other radiation devices, not including AEC units and nuclear power reactors, which are expected to increase in number. To these have been added the newer types of radiation hazards born of the atomic age. This combination of the new and old has brought about the need for public health protective measures.

The health department of a neighboring State has 58 men assigned to its radiation program, and these could adequately inspect only 1,500 X-ray units a year. On that basis it would take more than 400 employees to check annually all units in Ohio. Obviously, this is impossible. We must look to local health departments to help us take on this new task and we, in turn, will help them to assist us.

Despite many advantages, the suburban spread has emerged as a challenge to public health. Food and water supply, sewers, and waste disposal are among the new aspects of environmental sanitation for which we are seeking a solution. Transportation and communication difficulties are added to those of medical care, emergency treatment, and clinical and hospital services, all of which are more easily solved in metropolitan areas.

Though the new suburban life undoubtedly provides an emotionally healthful one, enabling people as it does to get away from the polluted atmosphere, noise, traffic hazards, and other tribulations of urban living, public health departments must be on their toes to keep the scales favorably balanced and not let the advantages become lost under an accumulation of liabilities.

The responsibilities and activities in public health I have cited are by no means complete and inclusive, but only examples of the definite growth pattern. All of us in the public health field stand to gain by working together, and professional organizations such as our own Ohio Public Health Association give us individual and united strength for the new tasks ahead.

Culture, Society, and Health

brief

Three general areas in which variables of society and culture and public health meet are disease and health; institutions, agencies, procedures, and personnel; and behavior, attitudes, and values (*1*).

Virtually all mass disease has social and cul-

tural correlates, that is, has to do in part with the way people behave, think, and adjust. Further, the means developed by society for the control of disease and promotion of health—as well as what people think and do about health and programs designed to promote public health—are profoundly immersed in social and cultural factors.

Each of these general areas is illustrated in the following examples.

Work Simplification

Local heart associations have sponsored classes to teach housewives with cardiovascular and other disabling conditions how to simplify their domestic work. The work-simplification principles were worked out by Mrs. Frank B. Gilbreth, wife of the co-author of "Cheaper by the Dozen." Several years ago, I was asked to help evaluate a series of such classes in the Boston area. The evaluation consisted of asking the women who had attended the classes, some weeks after the series had ended, what they thought of the classes, whether they had applied any of the principles of work simplification; if so, with what results, and if not, why not. The findings gained from interviews were extremely variable. A few women had apparently gained and applied a good deal; they had modified many operations in kitchen, laundry, and general housekeeping. Some women had apparently gained nothing; at any rate, they had not altered their domestic routines appreciably. Others fell in-between, but mainly toward the extreme of the least gain. It seemed, on first analysis, that the highly uneven and, on the whole, not very encouraging results of the classes might be due simply to fortuitous individual differences.

Whether or not this conclusion is warranted, these uneven results indicate that studies of the cultural patterning and meaning of housework are needed before such teaching can be maximally effective. For instance, at what points for women of different backgrounds do cleaning the kitchen, doing laundry, making beds, preparing various foods, and the like, begin and end? What variations occur in "cut-off" points between one activity and another? By what systems of domestic priorities do women of different groups abide? What is housework, as viewed by different groups?

Staphylococcal Infections

Staphylococcal infection in hospitals has become important as a public health matter. Tibbitts, Demerath, and Wessen (*2*) point out that there are some well-known and some overlooked social and cultural correlates of hospital-borne staphylococcal infection.

It is known that the staphylococcus is normal to the flora of man and is found on the skin, in nasopharyngeal passages, and in the gastrointestinal tract. It appears that staphylococcus may be transmissible by ventilation systems as well as by personal contact. Only under certain circumstances, possibly host determined, is it pathogenic. Many strains have been identified, most of which can produce disease when the host's defenses are lowered. Some strains have acquired resistance to antibiotics; these strains are isolated most frequently in outbreaks. The organism is characterized by a very large gene pool and hence is highly variable biochemically. New variants constantly are emerging.

The widespread distribution of the staphylococcal organism and the fact that not all those exposed to it acquire the disease invite comparison with the tubercle bacillus, which is also ubiquitous but does not have the same effect on all those exposed to it.

Here is an opportunity for sociologists to collaborate with epidemiologists. Pertinent social variables include demographic characteristics of the affected population and incidence in the social space of family, community, or hospital, with consideration being given to positions, quality of the social relations, hygienic practices, and values and attitudes of individuals or social categories which are affected. Because of the ubiquitous character of the organism, it might be highly profitable to study within social groups differences between individuals who are and are not stricken, given common exposure, as nearly as this can be determined.

There is need to explore differing perceptions

Based on a paper by Edward Wellin, Ph.D., director, behavioral sciences activities, American Public Health Association.

of the staphylococcal problem between nurses and physicians, surgeons and nonsurgeons, and administrators, supervisors, and others in hospital organizations. These might pertain to the sources-of-control ideas, the kind of control measures considered and adopted by hospital administrators, and the likely sources and mechanisms of infection. It might be revealing to explore the relation to infection rates of structures of authority and influence or of the correspondence between formal and informal patterns of communication. The effectiveness of a hospital committee on infections could be studied in relation to the composition of the committee.

New Issues in Fluoridation

In 1945, the water of Newburgh, N.Y., was fluoridated and that of Kingston, N.Y., left unfluoridated. Ten years later, Dr. D. B. Ast and colleagues published definitive reports which demonstrated that all children through 16 years of age in Newburgh had remarkably lower DMF ratios than children of Kingston. Children exposed to fluoridated water from birth had almost 60 percent fewer decayed, missing, and filled teeth than their Kingston counterparts, and children who had been exposed to fluorides from age 6 had 40 percent fewer DMF teeth than the controls.

But Newburgh children varied among themselves in regard to DMF ratios. What accounted for this variation? Of course, we know that a series of individuals exposed to the same stimulus will vary in reaction to it. But the prior question is: Were they all equally exposed to the same stimulus? Although the tapwater in each Newburgh residence was presumably equally fluoridated, the question we cannot answer is whether all children got equal doses and equal frequencies of dosage of the fluoridated water. The likelihood is that just as people vary in other behaviors, they vary in patterns and frequencies of water intake.

Now consider the implications of another study. This was an investigation in Contra Costa County, Calif., carried out in 1953–54 and reported by Donald J. Galagan and colleagues in the June 1957 issue of *Public Health Reports*. They investigated the fluid intakes generally and water intakes specifically of children from under 1 year to 10 years of age. The study sampled an entire year and its climatic changes. On water intake, measuring ounces of water per day per pound of body weight, the means for each sex and for age groups within each sex varied somewhat, but generally in an orderly way. The standard deviations, however, varied so much that there were obviously considerable differences in the range of water intakes. The mean intakes of all boys of one age compared with the means for other ages and with girls certainly told us something. But the mean is a measure of central tendency; it does not tell much about the spread. The spread, or standard deviation, was so great that it was obvious that some children were drinking more than the average amount of water for their ages and body weights, and others were drinking less.

Putting both studies together, that of Kingston-Newburgh on fluoridation experience and that of Contra Costa County on water intake by children, a new question is posed. Is there a relationship between variations in dental caries in a child population receiving fluoridated water and variations in water intake? In other words, if you lead the child to fluoridated water, are you sure that he will drink, and do you really know how much he will drink?

How much water, as distinct from fluids in which fluoridated water is not present, do children of different social classes, ages, and of each sex consume? Some communities have recently instituted fluoridation of water supplies and others will do so in the future. We need studies, particularly in these communities, which relate water-intake patterns to dental status following fluoridation. Social groups in the community differ in food habits, health attitudes, and other things; it would be rather surprising if they did not differ in regard to water intake.

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Family Group Therapy

To find an adequate treatment method for the disturbed adolescent is one of the major problems in psychotherapy. Conducting therapy with this age group has been so difficult that many have said we should not try to treat adolescents, and that when a child has reached 10 or 11 years of age we should modify his situation but postpone the attempt to do psychotherapy with him until he becomes an adult.

It is not through lack of trying psychotherapy that we have failed with children in this developmental stage. Psychoanalysis, which has had notable success in a few reported cases, has not proved, in general, a very useful method for this age. In most instances the ambivalence of the adolescent toward the therapist as toward all adults has made it difficult for the therapist to establish and maintain a therapeutic relationship within which the adolescent could examine his own difficulties and learn to adapt in new ways. The modifications of psychoanalysis in which the therapist has become more directive, more of a reality figure for the patient, have been reported to be more effective. But apparently the success has not been sufficient to encourage widespread adoption of this approach. Therapy with groups of adolescents, which has been utilized more and more commonly of late, has been advocated as a therapy of choice for their age. Complementary groups composed of the parents of adolescents have been urged as desirable supplements to the adolescent groups. These and similar approaches have not filled the need for effective therapeutic method, for in many cases the results they have produced have been less than gratifying.

It was against this background of some urgency that the method of treatment called "family group therapy" was developed.

Family group therapy is an effort to effect behavioral and attitudinal changes within a total family through a series of conferences attended by the parents, the children 9 years of age and older, and the therapist. In most instances the conferences are initiated through referral of a child who is disturbed, but from the beginning the therapeutic goals are family-centered rather than child-centered. The primary intent of the therapist is to accomplish a modification of the functioning and structure of the family as a group. It is assumed that as a consequence modifications will be effectuated secondarily in the situation of individuals within the family. The method of the therapy emerges, then, from the one basic assumption differentiating it from individual therapy: the family is the unit to be treated.

It is important to stress that in this method the family is not regarded as an assembly of individuals, but is recognized as a biological and social unit. One must keep in mind that

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Public Health Monograph No. 64

Family Group Therapy. *By John Elderkin Bell.* Public Health Monograph No. 64 (PHS Pub. No. 826), 52 pages. U.S. Government Printing Office, Washington, D.C., 1961, price 35 cents.

The accompanying text presents the basis for family group therapy which is described in detail in Public Health Monograph No. 64, published concurrently with this issue of *Public Health Reports.* The author is mental health consultant in psychology and acting chief, Mental Health Services, Public Health Service, in Region IX of the U.S. Department of Health, Education, and Welfare.

For readers wishing the data in full, copies are on sale by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. Official agencies and others directly concerned may obtain single sample copies without charge from the Public Inquiries Branch, Office of Information, Public Health Service. Copies will be found also in the libraries of professional schools and the major universities and in selected public libraries.

here no child or parent is under treatment as an individual. Whereas in individual therapy the emphasis is on the unique person, in family therapy specific attention to the individual as an individual is to be avoided as much as possible. The problem for which the family is accepted for treatment is to be thought of as a problem of the family, not as a problem of the child. Those who are accustomed to individual therapy may find the shift to emphasis on the family as a unit a difficult change in orientation.

Specifically, emphasis on the family means that the problem for which the family comes to treatment must be accepted not as the symptom of an individual's disturbance but as a symptom of disrupted relationships in the family. The hypothesis that lies behind the therapy for both child and parent in the traditional clinic, namely, that where there is a disturbed child there are disturbed parents, is reinterpreted. The hypothesis is now made that where there is a disturbed child there is a disturbed family. This leads to a series of theoretical consequences culminating in the conclusion that all members of the family contribute to the disturbance. Whereas etiologically it may be true that the parents were disturbed first, in the present they are not judged individually as either more or less responsible for the disturbance than others in the family. Thus it is not important to try to decide whether this parent is good or that parent is bad. What each parent and each child may be is the result of the family totality. It is no more useful to say the parents are responsible for the child's difficulties than to say the child is responsible for the parents' problems. To continue to think in traditional terms will handicap the therapist, who must learn to think of the family as an organic unit.

Functionally, then, the symptom is thought of as the product of a disruption in family interaction, most usually a breakdown in intrafamily communication, and not as the product of intrapsychic conflicts. From this point of view conflicts within the individual become the end results rather than the causes of disturbance. The normal interpretation of what is symptomatic is thus modifed.

A further implication of the basic assumption relates to the goals of the therapy. The goals may represent the values of the therapist, but it is more likely that they emerge primarily from the matrix of cultural norms established within the subculture of which the individual problem family is a part. Consciously the therapist seeks to improve the means by which interaction may take place within the family. This is at least a twofold process: first, of releasing the respective members of the family from inhibition about the expression of feelings, wishes, ideals, goals, and values, and second, of developing new forms of expression to channel the interpersonal communication. To increase spontaneity is only one side of the picture; the other is to pattern the more spontaneous activities so that the perpetuation of activities that are helpful to the family's purposes is facilitated and the change of interactions that may retard the needed growth of family life is accomplished. We can say, then, that both release and discipline are goals of the therapy.

A further goal of the therapy is to make the family conscious of the roles that the various members play in relation to one another. It might be expected that changing these roles would be a major aim, but that is not necessarily so. Many of the forms of behavior that grow out of the roles appropriated by the members of the family are desirable to the family and to the individuals in the family, who must retain the option of continuing or discarding these roles.

A third goal is to demonstrate to the family its essential unity and thus the mutual interdependence of each with the other and with the family as a whole. The strength of the cohesive forces within most families makes it seem natural to both the parents and the children that the family should examine its status and rethink its fortunes in the family therapy conferences. In spite of the tacit recognition of these bonds, the members of a disturbed family are more likely to be aware of the divisions, the tensions, and the hostilities they experience with one another and of their symptomatic expression. In the course of the therapy there is a reaffirmation of the meaning of the family to each.

Federal Publications

The National Water Quality Network, 1960. *PHS Publication No. 663; 1961; 436 pages.*

Data on water quality are compiled from reports of the expanded network of sampling stations. A streamflow section has been added in this edition. Tables on radioactivity, plankton population, and organic chemical and chemical, physical, and bacteriological analyses have been continued.

Sewage and Water Works Construction, 1960. *PHS Publication No. 758; 1961; 24 pages.*

Basic data on contract awards are tabulated for sewage treatment works, collecting sewer construction, sewer construction, waterworks construction, and combination construction. Analyses are given of population size groups and drainage basins and by States and contract size groups.

Public Health and Clean Water. *PHS Publication No. 828; 1961; 7 pages.* A review of the "microchemical era of public health" condensed from an address by Gordon Fair, professor of sanitary engineering at Harvard University.

Clean Water, A National Resource. *PHS Publication No. 828C; 1961; 10 pages; 10 cents.* Outlines water needs for the future against a historical background of public health.

Recreation and Clean Water. *PHS Publication No. 828A; 1961; 5 pages; 5 cents.* Stresses the dangers in polluted waters to all forms of water-oriented recreation and cites many examples of "our vanishing shoreline" in a time of social change when outdoor recreation is becoming a major feature of American living.

Fish, Wildlife, and Clean Water. *PHS Publication No. 828B; 1961; 8 pages; 5 cents.* Discusses stream pollution by industrial, chemical, and domestic wastes and effects on fish, wildlife, and man.

Municipal Water Facilities Inventory as of January 1, 1958. *PHS Publication No. 775, Vols. 1–9; 1960, 1961.*

Detailed information is tabulated on all water facilities in communities with a 1950 population of 100 or more. The volume numbers correspond to the Department of Health, Education, and Welfare regions. Data for each State are also bound separately.

The Psychopharmacology Service Center. *PHS Publication No. 809. December 1960; leaflet; 10 cents.*

Describes activities of the Center at the National Institute of Mental Health and its research grant program in psychopharmacology. Cites areas in which research is currently underway, grant procedures, activities for which grant funds may be used, and consultative and informational services provided investigators.

Hospital Equipment Planning Guide. *PHS Publication No. 822; revised 1959; 56 pages; 35 cents.*

This guide, revised periodically and used extensively by hospital planners, includes steps in preparing an equipment list, sample forms, estimated average costs, and suggested equipment for 50-, 100-, and 200-bed general hospitals.

The Dog in Medical Research. *PHS Publication No. 312; revised 1961; by Keith S. Grimson; 15 pages; 15 cents.*

This guide, written primarily for investigators with projects requiring dogs, discusses physical and ethical standards for the care and maintenance of dogs used for experiments. Contents include sections on sources of animals, selection for special purposes, care and handling, quarters, feeding, and humane treatment. A list of guiding principles is featured, as well as a model pound law for local jurisdiction. New with this edition are the section on humane treatment and a list of organizations interested in the care of laboratory animals.

Highlights of Progress in Mental Health Research, 1960. *PHS Publication No. 824; 1961; 43 pages; 25 cents.*

Items on programs and research studies conducted and supported by the National Institute of Mental Health are grouped under ten subject headings: progress in treatment, biological studies, psychopharmacology, childhood studies, aging, delinquency, suicide, retardation, drug addiction, and alcoholism.

Basic research at both the biological and psychological levels as well as clinical and sociocultural programs and projects is included. General summary statements introduce most subject areas.

About Syphilis and Gonorrhea. *PHS Publication No. 410 (Health Information Series No. 84); leaflet; revised 1961; 5 cents, $2.50 per 100.* Describes symptoms of diseases, dangers to the affected person and offspring, and methods of transmitting. Cautions against self-treatment, pills, salves, and quacks. Stresses immediate care by a doctor or public health clinic.

This section carries announcements of new publications prepared by the Public Health Service and of selected publications prepared with Federal support.

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